‘A STUDY TO ASSESS SERUM CALCIUM AND ALKALINE PHOSPHATASE LEVELS IN PATIENTS ON ANTIEPILEPTICS IN GOVERNMENT VELLORE MEDICAL COLLEGE HOSPITAL,VELLORE.’

A DISSERTATION SUBMITTED TO

THE TAMILNADU DR.M.G.R MEDICAL UNIVERSITY

In partial fulfillment of the regulations for the award of the degree of

M.D. GENERAL MEDICINE – BRANCH I

DEPARTMENT OF GENERAL MEDICINE

GOVERNMENT VELLORE MEDICAL COLLEGE AND HOSPITAL

THE TAMILNADU DR.M.G.R MEDICAL UNIVERSITY

CHENNAI

APRIL 2019

CERTIFICATE

This is to certify that the dissertation titled **"A STUDY TO ASSESS SERUM CALCIUM AND ALKALINE PHOSPHATASE LEVELS IN PATIENTS ON ANTIEPILEPTICSIN GOVERNMENT VELLORE MEDICAL COLLEGE HOSPITAL, VELLORE"** is a genuine work done **BY DR. NANDHINI DEVI. D,** Post Graduate student (2016 – 2019) inthe Department of General Medicine, Government Vellore Medical College, Vellore under the guidance of **Prof. Dr. R.THILAKAVATHI M.D.,DCH.,**

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INSTITUTIONAL ETHICAL COMMITTEE

APPROVAL CERTIFICATE

GOVT. VELLORE MEDICAL COLLEGE, VELLORE-11

Title of the Study	–	A study to assess serum calcium and alkaline phosphatase levels in patients on Antiepileptics in GVMCH.
Principal Investigator	–	Dr.D.Nandhini Devi, Post Graduate M.D(GM)., GVMC, Vellore-11
Guide	–	Dr.K.Thilakavathi MD., Associate Professor, Dept of General Medicine, GVMC, Vellore

The request for an approval from the Institutional Ethical committee (IEC) was considered on the IEC meeting held on 12.10.2017 at the Conference Hall, Govt. Vellore Medical College, Vellore-11.

The members of the committee, the secretary, the Convenor and the President are pleased to approve the proposed work mentioned above submitted by the Principal Investigator.

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CERTIFICATE – II

This is to certify that this dissertation work titled **'A STUDY TO ASSESS SERUM CALCIUM AND ALKALINE PHOSPHATASE LEVELS IN PATIENTS ON ANTIEPILEPTICS IN GOVERNMENT VELLORE MEDICAL COLLEGE HOSPITAL, VELLORE'** of the candidate **DR. D. NANDHINI DEVI** with registration Number **201611653** for the award of **M.D. DEGREE** in the branch of **GENERAL MEDICINE**. I personally verified the urkund.com website for the purpose of plagiarism Check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows **2%** percentage of plagiarism in the dissertation.

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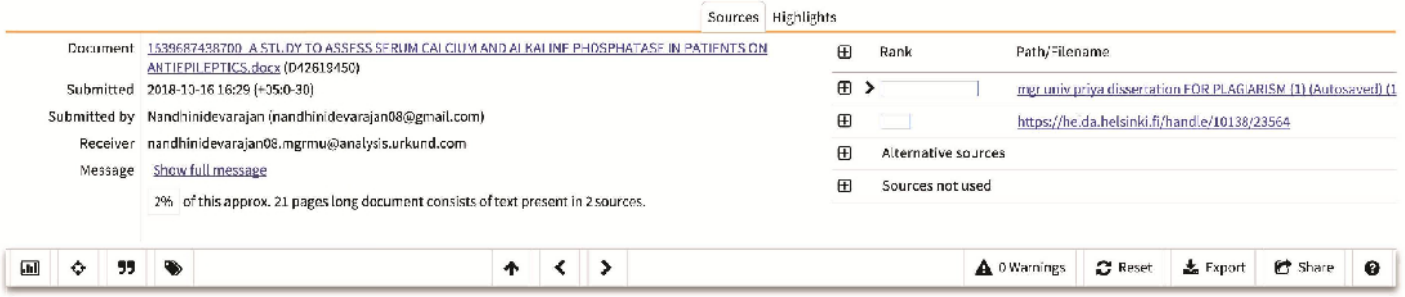

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THE TAMILNADU DR.M.G.R MEDICAL UNIVERSITY CHENNAI APRIL 2019 INTRODUCTION
Epilepsy is an important public health problem and the second most common neurological problem next to headache [1]. In worldwide and in India its prevalence is

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DECLARATION

I, **DR. D. NANDHINI DEVI** solemnly declare that this dissertation titled '**A STUDY TO ASSESS SERUM CALCIUM AND ALKALINE PHOSPHATASE LEVELS IN PATIENTS ON ANTIEPILEPTICS IN GOVERNMENT VELLORE MEDICAL COLLEGE HOSPITAL, VELLORE'** is a bonafide work done by me in Department of General Medicine, Government Vellore Medical College And Hospital, Vellore under the guidance and supervision of **Prof. Dr.R.THILAKAVATHI M.D.,DCH.,**

This dissertation is submitted to the Tamilnadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the university regulation for the award of M.D., Degree in General Medicine (Branch – 1).

Place : Vellore

Date : DR. NANDHINI DEVI D

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ABBREVIATIONS

AEDs - Antiepileptic Drugs

PTH - Parathyroid Hormone

PHT - Phenytoin

CBZ - Carbamazepine

SVP - Sodium Valproate

PB - Phenobarbitone

CNS - Central Nervous System

BMD - Bone Mineral Density

SHBG - Sex Hormone Binding Globulin

VPA - Valproic Acid

PICP - Type I Procollagen C-Terminal Peptide

NTX - N-Telopeptide Of Type I Collagen

ICTP - Carboxy-Terminal Telopeptide Of Type I Collagen

PXR - Pregnane X Receptor

BMI - Body Mass Index

ILAE - International League Against Epilepsy

SGOT – Serum glutamic oxaloacetic transaminase.

SGPT - Serum glutamic pyruvic transaminase

TABLE OF CONTENTS

INTRODUCTION

Epilepsy is an important public health problem and the second most common neurological problem next to headache(1). In worldwide and in India its prevalence is about 50 million and 10 million persons respectively according to WORLD HEALTH ORGANISATION(2–4). It is defined as two or more episodes of unprovoked seizures by ILAE(4). Epilepsy is the disorder of the brain characterised by a predisposition to develop seizures. Antiepileptic medications remains the main line of treatment for a patient with epilepsy. Antiepileptic medications can cause acute and chronic adverse effects with greater impact on quality of life(5). Evidence suggest association between AED's and bone mineral abnormalities(6).Due to abnormalities in bone mineral metabolism caused by these drugs , taking them for longer period of time without adequate supplementation imposes increased risk of fractures(7) and bone loss (osteomalacia) thereby affecting the health and quality of life . The bone mineral abnormalities commonly (8,9)observed are

- Hypocalcaemia,
- Hypophosphatemia,
- Increased PTH
- Increased Alkaline Phosphatase,
- Evidence Of Bone Loss On X- Ray.
- Decreased levels of active vitamin D metabolites

The drugs commonly associated with these risk are phenytoin, phenobarbitone, carbamazepine and sodium valproate. These drugs are potent inducers of ***CYTOCHROME P 450***(10–13). The induction of these enzymes leads to conversion

of vitamin D into inactive metabolites thereby decreasing vitamin D mediated intestinal calcium absorption.

Other possible mechanisms for affecting bone health are

- Direct Inhibition Of Intestinal Calcium Absorption
- End Organ Resistance To Vitamin D And PTH.

Studies have been reported from 1960's by **KRUSE ET AL**(14)**, RICHEN AND ROWE ET AL**(15)**, DENT ET AL**(16)**, etc** about the effects of the antiepileptic medications on bone health and mineral homeostasis. In various national and international studies being reported for the past four decades, the prevalence of hypocalcemia was estimated to be 3 to 30%(17) and that of increased alkaline phosphatase was 27 to 41 %(18) which is a marker of increased bone turnover caused by bone loss. The hypocalcemia will lead to secondary hyperparathyroidism. The severity of these abnormalities is determined by the duration of therapy and number of drugs taken.

Hypocalcaemia is defined as the serum calcium levels less than 8.5 mg/dl and alkaline phosphatase levels more than 140 IU/L is considered high. Since the problem is subclinical , patients are unaware about the bone loss and their increased risk for fractures.

So studies have proved that supplementing these patients with calcium and vitamin D analogs will reduce the risk of fractures and bone loss by enduring adequate strength to bone and by maintaining mineral homeostasis.(19)

Our study focuses about comparing the levels of calcium and alkaline phosphatase in patients on antiepileptics and those not on antiepileptics in an

outpatient basis and also to assess the prevalence of hypocalcemia among patients on antiepileptic therapy. The data obtained from the study will help us to determine the need for calcium and vitamin D supplementation in patients on chronic antiepileptic therapy to avoid the risk of fractures and monitor them periodically with the help of these markers of bone health to avoid the complications.

REVIEW OF LITERATURE

Epilepsy is an important public health problem with more than 50 million people affected by the disease throughout the world(2). It is the second most common neurological condition that stands next to headache.(1) This disorder necessitates the patients to be on antiepileptic therapy that includes enzyme inducing (phenytoin, phenobarbitone, carbamazepine) and non enzyme inducing drugs. The treatment with antiepileptic agents is often chronic. AED's can cause acute and chronic adverse effects that can affect the quality of people's life. The longer duration of therapy is associated with abnormalities of bone ranging from decrease in mineral metabolism of bone to decrease in bone mineral density and fracture risk(6). Their fracture risk is increased by 2 to 6 times compared to general population(7).

Although studies have been reported about the risk of bone disease in patients on antiepileptic therapy in institutionalised patients due to lack of nutrition and factors like sunlight exposure, in the past four decades, articles about the risk of it in ambulatory patients has also been(20) published.

In the year 1968 in a study conducted by **KRUSE**(14)**,** he has reported abnormalities in the levels of calcium, alkaline phosphatase and phosphate , with X ray evidence of osteomalcia in about 15% of children taking antiepileptic therapy. The severity of the disease is determined by the number of drugs taken and duration of the therapy(15).

In a study conducted by Petty et al(21), prevalence of clinical or subclinical bone disorders was more than 50% in patients on chronic antiepileptic medications.

The common abnormalities observed with antiepileptic therapies are:

1. Hypocalcemia.
2. Increased alkaline phosphatase.
3. Increased parathyroid hormone.
4. Hypophosphatemia.
5. Reduced levels of biologically active vitamin D metabolites.
6. Radiologic evidence of rickets .
7. Histologic evidence of osteomalacia.

Enzyme inducing antiepileptic drugs like phenytoin, phenobarbitone, carbamazepine, primodine are known to cause these side effects.

PREVALANCE OF EPILEPSY WORLDWIDE:

The prevalence of epilepsy in the world is estimated to be 50 million worldwide at any given time(4). Prevalence and incidence of epilepsy differs by demographic factors like age, race, sex and socioeconomic status. In developing countries,the likelihood of epilepsy is more in adolescence and adults. In developed countries it increases as age increases. With relation to sex, males are reported to be more than females (1)because females tend to conceal their symptoms and diagnosis due to beliefs. Prevalence of epilepsy is more in people with low socioeconomic status because of poor health conditions.

EPILEPSY IN INDIA:

According to world health organisation, About 10 million persons with epilepsy are estimated to be present in India with a prevalence ofabout 1%. In **Bangalore Urban Rural Neuro Epidemiological Survey (BURNS)**, it was observed in various studies that the prevalence rate of epilepsy was 5 to 10/1000 population, among which rate in rural areas is higher than that in urban areas. In a study conducted by **BHARUCHA et al**(22)**,** males are significantly higher than females according to the prevalence rates.

DEFINITION OF EPILEPSY:

Defined as a condition characterised by two or more episodes of seizures due to unprovoked causes according to INTERNATIONAL LEAGUE AGAINST EPILEPSY (ILAE 1993).

The term seizure, a latin word (meaning - to take possession of) is a sudden unexpected event due to abnormal neuronal activity in the brain. It is manifested as episodes ranging from events indistinguishable by the observer to obvious convulsive activity. It can be provoked (due to underlying structural or metabolic causes) or unprovoked.

CLASSIFICATION OF SEIZURES :

Based on electrical and clinical activities seizures are classified into 2 major types:

- **FOCAL**
- **GENERALISED**

- FOCAL - arises in certain areas within cerebral hemispheres and limited to the same. Mostly due to structural problems in the brain.
- GENERALISED: arises within and spreads rapidly across cerebral hemispheres. Mostly due to cellular, biochemical or structural causes.

SUBCLASSIFICATION:

Focal seizures

(Can be further described as having motor, sensory, autonomic, cognitive or other features).

Generalized seizures

a. Absence – typical and antitypical

b. Tonic

c. Clonic

d. Tonic - clonic

e. Atonic

f. Myoclonic

- May be focal, generalized, or unclear

Epileptic spasms.

CAUSES OF SEIZURES:

Seizures occurs as a result of loss of balance between excitation and inhibition in the CNS. Clinical observations have stressed that various factors influence conditions that can cause seizures or epilepsy

1. Certain endogenous factors can determine the development of seizures in appropriate situations by reducing its threshold. Ex: febrile seizures.
2. EPILEPTOGENIC FACTORS - which converts the normal neurons of the brain into hyperexcitable ones. Some of them are infections, trauma, stroke, developmental anomalies,etc..
3. PRECIPITATING FACTORS: certain factors can precipitate seizures in epileptic or non epileptic. Like deprived sleep, stress, toxin or drug exposure.

ANTIEPILEPTIC THERAPY:

Patients diagnosed with epilepsy are started on antiepileptic therapy irrespective of the cause. It is the mainstay of treatment for all patients in controlling the further episodes of the seizures. Duration of treatment with these drugs are usually for chronic period of time and this imposes the patient on risk for fractures, bone loss due to abnormalities in the bone mineral metabolism(6,7). The risk for bone loss is determined by the duration of therapy and number of drugs taken. Studies have been reported that the bone loss begins within 3 to 6 months of starting the therapy(19).

The antiepileptic drugs encompasses a variety of drugs with different mechanism of actions. Among the antiepileptics used, some are potent inducers of cytochrome P - 450 enzymes and some of them are inhibitors of it. First line drugs like phenytoin, phenobarbitone, carbamazepine and primidone are potent inducers and sodium valproate is an inhibitor.

New generation drugs like topiramate, levecetiracetam,zonisamide,lamotrigine (23)etc are not enzyme inducers and thus are not associated with abnormalities of mineral metabolism.

In India, phenytoin, phenobarbitone, sodium valproate and carbamazepine are the first line and commonly used drugs in government hospitals.

MECHANISM OF ACTION :

PHENYTOIN:

- It limits the spread of seizure activity with maximum effect on tonic phase of convulsive seizures.
- It stabilises the neuronal membrane and prevents repetitive detonation by prolonging the inactivated state of voltage sensitive neuronal Na+ channel.
- Inhibits high frequency discharges.
- Other mechanism – inhibition of glutamate, reduction of calcium influx
- Dosage - 300 to 400 mg/ day
- Metabolised by CYP2C9
- Side effects:
    1. Gum hypertrophy, Megaloblastic Anaemia
    2. Osteomalacia
    3. Hirsutism
    4. Skin rash and Lymphadenopathy
    5. Neurologic – dizziness diplopia, incoordination

- **CARBAMAZEPINE:**It acts by prolonging the inactivated state of neuronal Na+channel.
- Metabolised by **CYP2CP** and potent inducer of **CYP3A4**
- DOSE – 600 to 1800 mg/day
- Side effects

1. Ataxia
2. Aplastic anaemia and Leucopenia
3. Gastrointestinal irritation, Obstructive Jaundice
4. Hyponatremia
5. Osteomalcia

PHENOBARBITONE:

- Acts by enhancement of GABA mediated synaptic inhibition
- Dose – 60 to 180 mg/day
- Side effects:

1. Sedation
2. Ataxia
3. Confusion
4. Skin rash
5. Osteomalacia

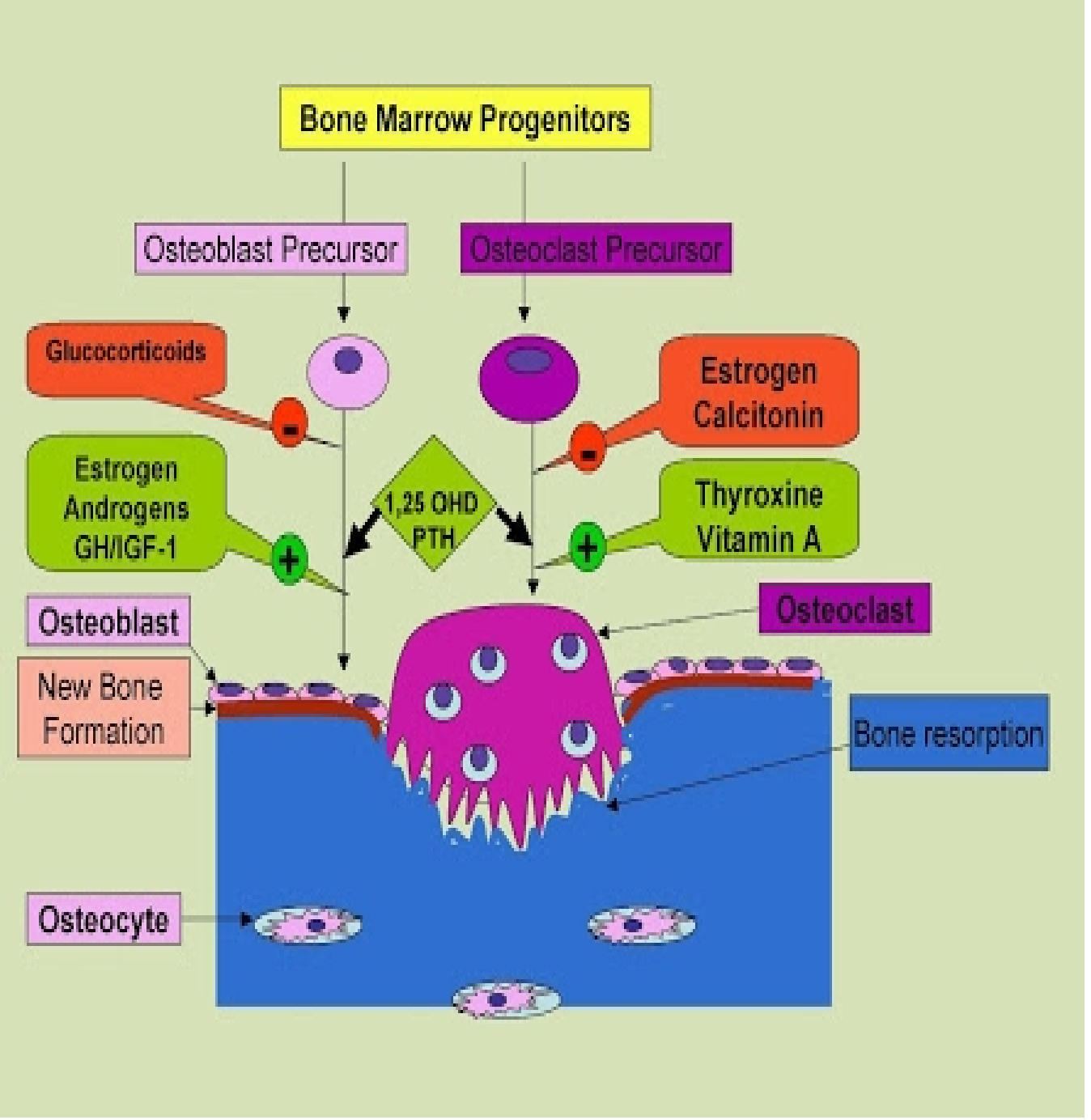


FIG 1 – Showing Development of osteoblasts and osteoclasts from bone marrow progenitors and factors affecting it. PTH: Parathyroid Hormone, GH – Growth Hormone, IGF – Insulin Like Growth Factor

BONE STRUCTURE AND METABOLISM:

Bone is a modified dynamic tissue that is continuously remodelled throughout life.

Bone is made up of three types of specialised cells:

Osteoblasts – that initiates bone formation

Osteocytes – monitors bone progress

Osteoclasts – initiates bone reabsorption

BONE MATRIX:

- **Inorganic** – constitutes bone minerals.

  60 to 70% of bone weight.

  Formed by calcium and phosphorus predominantly.

- **Organic –** includes collagenous and non collagenous matrix.

- **Collagenous**

  forms 30% of dry bone weight.

  Made of type 1 collagen (90%) and small amount by type 4 collagen.

- **Noncollagenous** -

Includes osteopontin, calcium binding proteins like matrix glaprotein and osteocalcin, thrombospondin, bone specific alkaline phosphatase, bone morphogenetic protein.

The functions of the osteoblasts are controlled by a variety of minerals like calcium, phosphorus and hormones like Insulin like growth factor 1 and 2, PTH, vitamin D3.

BIOCHEMICAL MARKERS FOR BONE REMODELLING :

- Divided into makers of bone formation mediated by osteoblasts and markers of bone resorption which represents osteoclastic activity.
- Osteoblast activity is reflected by increased levels of alkaline phosphatase, type I procollagen C-terminal peptide (PICP) and osteocalcin which serves as markers of bone formation.
- Bone resorption markers are urinary hydroxyproline, hydroxylysine.
- Alkaline phosphatase is the most common marker for bone formation although it is present as two isoenzymes, bone and liver.
- Physiologically bone markers are elevated during growing age and bone repairs.

REGULATION OF BONE REMODELLING:

- Regulated by minerals like calcium and phosphorus and hormones like Vitamin D3, PTH, Insulin like growth factor 1and 2, sex hormones.
- To some extent ,nutrition and physical activity also influences remodelling.
- Medications like steroids , AED's and decreased estrogen in postmenopausal women are likely to induce bone loss, there by increasing risk of fractures.

EPILEPSY AND BONE:

Patients with epilepsy are prone for fractures due to various factors like use of AED's causing bone loss, falls during seizure activity and ataxia, giddiness and sedation caused by antiepileptic drugs can increase the risk of fracture.(24–26)

ANTIEPILEPTICS AND FACTORS AFFECTING BONE REMODELLING:

Adverse effects on bone by AED's is being reported from past four decades. It includes abnormalities like hypocalcemia , low vitamin D levels, increased PTH and low phosphate levels(27). These abnormalities are commonly found with enzyme inducing antiepileptics like PHT, CBZ, PB. These antiepilpetics produce these abnormalities by increasing the catabolism of vitamin D into inactive metabolites and also by affecting the cellular response to PTH. These above mechanisms has been proposed to increase bone turnover and to increase remodelling of bone. In addition PHT, also affects the direct intestinal calcium absorption and vitamin D mediated calcium absorption to some extent(27). Some of the studies showed no significant differences in calcium and phosphate levels in patients in chronic AED'S(28,29).
Sodium valproate being an enzyme inhibitor is known to affect the bone mineral metabolism by stimulating the osteoclast activity(30).

Increased levels of PTH has been reported in epileptic patients on chronic AED'S. This increase in PTH is likely to be a secondary response to low vitamin D levels.(11) However , studies reporting increased PTH levels without associated decrease in vitamin D levels has been published thereby suggesting mechanisms independent of vitamin D deficiency affecting bone metabolism by antiepileptics. High PTH levels increases the bone turnover and predisposes to decreased bone loss and osteomalacia.

Drugs like phenytoin and CBZ are known to induce osteomalacia by inhibiting the profileration of human osteoblast cells besides affecting calcium and vitamin D homeostasis.

Studies have reported low levels of active vitamin D metabolites in patients on chronic antiepileptic therapy due to induction of hepatic enzymes by enzyme inducing drugs like PHT,CBZ, PB(10–13)

ANTIEPILEPTICS AND BONE DENSITY:

A decrease in bone mineral density and secondary osteoporosis was observed in patients using AED'S(17). Bones commonly affected are the femur and lumbar vertebrae. The risk for osteoporosis is 1.7 to 3.8, for osteopenia 1.3 to 3.8 and fractures it is 1.7 to 6.1(31). The sequence is normal BMD to osteopenia to osteoporosis to fractures.

The risk factors for reduced BMD in epileptic patients are as follows:

- Reduced physical activity
- Lack of sunlight exposure
- Inadequate dietary intake of calcium
- Postmenopausal women
- Alcohol and smoking
- Concomitant intake of drugs like glucocorticoids, chemotherapy.
- Female gender.
- Intestinal malabsorption and liver diseases.
- Hyperthyroidism and hyperparathyroidism(32)

A study by **KULAK ET AL**(28) has reported 53.4% and 10.4% of osteopenia and osteoporosis respectively. These observations are common with enzyme inducing AED'S and for enzyme inhibitor like sodium valproate. In a few small studies new antiepileptics are also associated with bone loss.

ANTIEPILEPTICS AND BONE TURNOVER:

Studies have demonstrated increase in markers of bone remodelling with the use of antiepileptics more with enzyme inducing AED's(33–37) The markers are as follows:

BONE FORMATION MARKERS – like osteocalcin, PICP, total and bone specific alkaline phosphatase.

BONE RESORPTION MARKERS – like N-telopeptide of type I collagen (NTX) and carboxy-terminal telopeptide of type I collagen (ICTP) andurinary deoxypyridinolines.

The increased levels of these markers is associated with decrease in bone mass which is a contributing mechanism for fracture risk. Histological evidence has suggested that the bone disease is mainly due to increased bone turnover (38).

ANTIEPILEPTICS ASSOCIATED WITH BONE DISEASE:

The antiepileptics most commonly associated with bone mineral abnormalities are cytochrome enzyme inducing drugs like PHENYTOIN, PHENOBARBITONE, CARBAMAZEPINE, PRIMIDONE. Majority of the studies that has got published till date is about these medications.

Studies regarding enzyme inhibiting drug like sodium valproate is limited. But in a study conducted in patients taking long term valproate therapy found increased concentrations of serum calcium, low Vitamin D3 concentrations,reduced bone mineral density using DEXA scan and increased markers of bone resorption.

Newer antiepileptic drugs like lamotrigine, topiramate. Zonisamide etc.. are less likely to cause these abnormalities as they are not potent enzyme inducers. Studies with no clinical significance regarding these abnormalities have come up in past few years.

Polytherapy is associated with more abnormalities than single therapy. No single combination is proved to be significant in causing more disease.

MECHANISM OF BONE LOSS BY ANTIEPILEPTICS:

Studies have been reported about the effects of enzyme inducing antiepileptic drugs on bone mineral metabolism and bone loss from 1960's. Since then evidence of AED's causing metabolic, biochemical and radiological abnormalities has been reported . Enzyme inducing AED's may lead to catabolism of vitamin D and hypocalcemia . Several mechanisms have been postulated which are listed below :

- **Alteration of calcium metabolism :**
  - Reduced Intestinal Cation transport
  - Vitamin D mediated calcium absorption reduced
  - Intestinal calcium absorption decreased

- **<u>Vitamin D Inactivation</u> :**
  - Induction of Hepatic enzyme
  - Pregnane X Receptor activation
- Osteoblast inhibition
- Decreased calcitonin
- Vitamin K deficiency
- Altered sex steroid and SHBG metabolism
- Modulation of aromatase activity

- **Increased parathyroid hormone:**
  - Insufficiency of vitamin D
  - Reduced cellular response to parathyroid hormone

Several theories has been published about the possible mechanisms of AED's induced bone loss. Among that induction of hepatic enzymes leading to conversion of vitamin D into inactive polar metabolites is the principal mechanism. But for drugs like sodium valproate which is an inhibitor of hepatic microsomes this mechanism will not explain the findings.

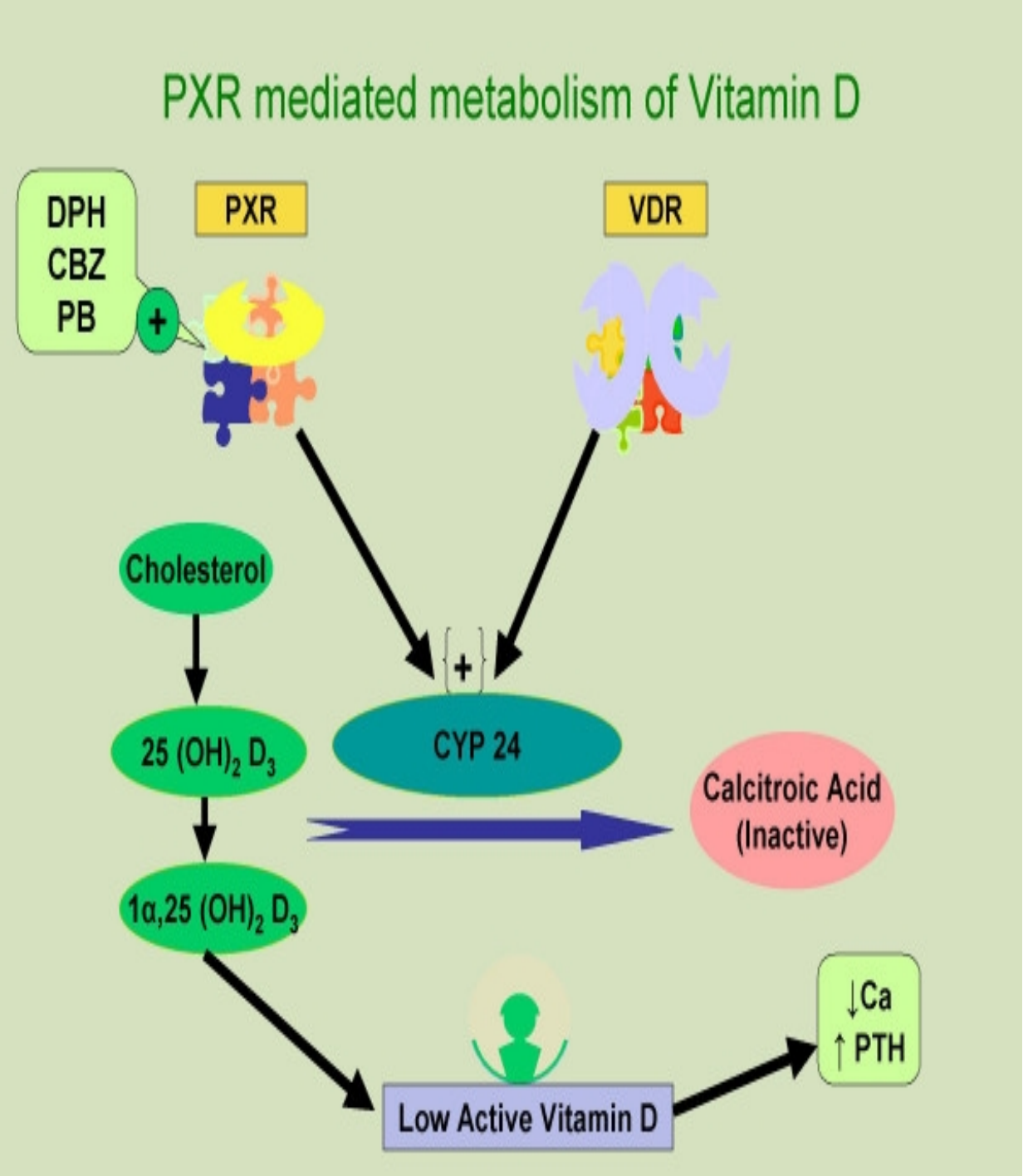
<u>AED'S AND CALCIUM:</u>

- It is postulated that enzyme inducing antiepileptic drugs like phenytoin, phenobarbitone, carbamazepine induces CYTOCHROME P450 which leads to catabolism of vitamin D into inactive polar metabolites thereby reducing biologically active vitamin D.

- Low levels of vitamin D causes hypocalcemia and hypophosphatemia due to decreased intestinal absorption and also increases the levels of parathyroid hormone leading to secondary hyperparathyroidism. PTH increases mobilisation of bone calcium stores and subsequent bone turnover. All these abnormalities leads to bone loss thereby increasing the risk of fractures.
- AED's especially PHENYTOIN may interfere with direct intestinal absorption of CALCIUM by mechanisms not clearly defined when tested in rats. In a study conducted by **BORSTEL SMITH ET**(39) published in the year 2007, effect of phenytoin on calcium transport in CaCO2 cells has been studied.

AED'S AND PXR:

- Pregnane X receptor shares homology in their DNA binding domain with vitamin D receptor . The PXR is expressed in intestine, kidney and bone.



The figure 2 depicts the effects of PXR on vitamin D metabolism

PXR – Pregnane X Receptor, DPH – diphenylhydantoin , PB – phenobarbitone, CBZ- carbamazepine.

- Drugs like phenytoin, phenobarbitone and carbamazepine are activators of PXR.
- Activation of PXR induces CYP 24 enzyme, that directs side chain oxidation and cleaves vitamin D3 into inactive metabolites thereby reducing active cellular concentrations of vitamin D inducing bone loss.(40,41)
- PXR also affects the osteoblast growth thereby affecting bone health apart from inactivating Vitamin D .

AED'S AND AROMATASE:

- Aromatase is an enzyme that functions in converting adrenal androgens to estrogens in peripheral tissues thereby maintaining the bone mineral density(42).
- Evidence from studies suggest positive correlation between BMD and estrone levels(42,43). So the above conversion by aromatase enzyme is essential.
- Aromatase is expressed in tissues like bone, liver , skin and gonadal tissues . Vitamin D3 is an important regulator of the enzyme and physiological concentrations of vitamin D3 is essential to maintain the ***aromatase activity in osteoblasts***(42).
- AED's by decreasing the active Vitamin D3 metabolites are known affect the aromatase activity.

AED'S AND SEX HORMONES:

- Hepatic enzyme inducing AED's are known to increase the catabolism of sex steroids and increase the synthesis of sex hormone binding globulin {SHBG}.

- AED's especially CBZ, VPA , PHT are reported to **inhibit synthesis of testosterone** from Leydig cells of testis(44)
- PHT and CBZ **increases the levels of sex hormone binding globulin** by increasing its synthesis, thereby reducing the levels of sex hormones like testosterone, DHEA and estrone.(45,46)
- PHT, CBZ and PB are known to **increase the clearance of circulating androgens**(45).
- All the above changes **reduces the activity of aromatase enzyme** by decreasing its androgen substrates and accelerates bone loss.(46–49)

AED'S AND VITAMIN K :

- Vitamin K is involved in posttranslational carboxylation of bone matrix proteins like osteocalcin(27). Phenytoin induced vitamin K deficiency causes bone loss by preventing the post translational modification. (9)

AED'S AND CALCITONIN:

- AED's are known to cause calcitonin deficiency. Calcitonin is a hormone produced by thyroid gland that inhibits osteoclast mediated bone resorption. Calcitonin deficiency therefore accelerates bone loss.

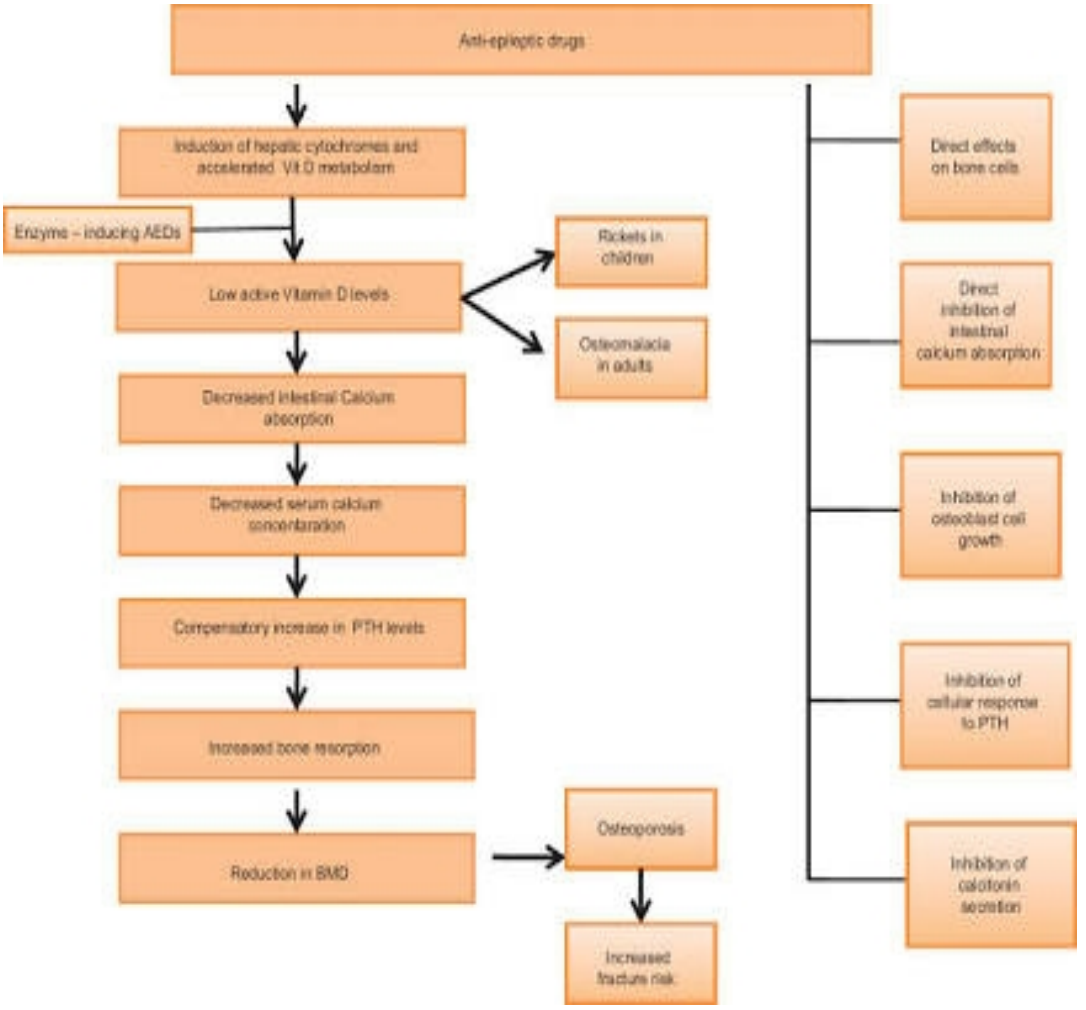
AED'S AND BONE CELLS:

- PHT and CBZ is reported to inhibit the profileration of human osteoblast like cell(50) and VPA is reported to act by stimulating osteoclast activity. PHT is shown to inhibit osteocalcin secretion from osteoblast(51).

Table 1-Bio chemical abnormalities of bone metabolism associated with AED'S:

FEATURES	***LEVELS IN SERUM/URINE***
CALCIUM	REDUCED IN THE SERUM
PHOSPHATE	REDUCED IN THE SERUM
25(OH)D3	REDUCED IN THE SERUM
PARATHYROID HORMONE	ELEVATED IN THE SERUM
MARKERS OF BONE FORMATION	ELEVATED IN THE SERUM
MARKERS OF BONE RESORPTION	ELEVATED IN THE SERUM/URINE

These are the postulated mechanisms by which AED'S are known to cause abnormalities of bone mineral metabolism and thereby increases the fracture risk.



The figure No: 3, depicts the effects of antiepileptic drugs on the bone mineral metabolism

PREVALENCE OF HYPOCALCEMIA IN PATIENTS ON AED'S:

The purpose of my study was to assess the prevalence of hypocalcemia in patients on antiepileptic therapy especially enzyme inducing AED'S. Various studies have reported the prevalence to be in the range of 3 to 30%. The calcium levels were in the subnormal levels not significant to cause symptoms.Studies have proved thatthe severity of hypocalcemia increases as the duration of therapyand number of drugs increases.(15,18)

CALCIUM AND BONE HOMEOSTASIS :

About 99% of calcium present in the human body is stored in the skeleton where it provides mechanical stability to the bone and serves as reservoir for maintaining extracellular calcium concentration at times..

Normal serum calcium level is **8.5 to 10.5 mg/dl** .

FORMS OF CALCIUM AND ITS FUNCTION:

It is present in two forms in the blood –

Ionised (50% of total calcium)

Non Ionised.

The ionised form is bound to negatively charged proteins like albumin, immunoglobulin, phosphate, citrate, sulfate, or other anions.

FUNCTIONS OF IONISED CALCIUM: .

i. Neuromuscular activity by helping in transmission of impulses
ii. Secretion of Hormones,
iii. Cardiac Contractility, and
iv. Coagulation of Blood.

ABSORPTION OF CALCIUM:

The daily requirement of calcium as suggested by institute of medicine is 1000 to 1200 mg for adults . The ingested calcium is absorbed mainly in the duodenum and proximal jejunum via active and passive transport. Passive (paracellular) transport is nonsaturable and contributes to 5% of daily calcium intake. Active transport is via ion channels **TRPV5 and TRPV6,** the expression of these ion channels is controlled by 1,25 (OH)2D. This form of absorption ranges from 20% to 70%.

REABSORPTION:

About 8 to 10g/d of calcium is filtered by the glomeruli. Of this, 65% is reabsorbed in proximal tubules via passive transport.

20% is reabsorbed in the cortical thick ascending loop of henle with the help of paracellin – 1. This reabsorption is inhibited by increased concentrations of calcium via calcium sensing receptor independent of parathyroid hormone or active vitamin D . Finally, 10% is reabsorbed in the distal convoluted tubule. The calcium enters the luminal surface of the cell via TRPV5. Ca- ATPases and Na+/ Ca2+ exchangers help in pushing the calcium across the basolateral surface. All these process are stimulated directly or indirectly by PTH and vitamin D.

REGULATION

The extracellular Calcium concentrations are maintained in the serum within a narrow range by the effects of parathyroid hormone, vitamin D and calcitonin.

❖ PARATHYROID HORMONE:

It is a 84 amino acid single chain peptide. Secreted by four parathyroid glands located on the posterior surface of the thyroid gland.

It is the principal regulator of extracellular calcium concentration in the blood. It acts directly on the bone and kidney and indirectly in the intestine via vitamin D to increase the calcium concentration in low states. Calcium acting through the calcium sensing receptor and vitamin D acting through the nuclear receptor regulates PTH synthesis and secretion.

ACTIONS OF PTH:

- **BONE** : stimulates both the osteoclasts and the osteoblasts . Stimulation of the osteoclasts results in bone demineralisation thereby increasing the calcium levels. Stimulation of osteoclast is indirect mediated by the cytokines released by the activated osteoblasts, because they lack receptors for PTH. Stimulation of the osteoblast will increase the bone remodelling. Hence , pulsatile secretion of parathormone increases bone remodelling through osteoblasts whereas sustained secretion will increase bone demineralisation through osteoclast activation.
- **KIDNEY** – decreases the renal clearance of calcium
- **INTESTINE**- increases calcium absorption in the intestine through the production of 1,25(OH)2D.

❖ VITAMIN D:

Vitamin D3 is the major steroid hormone involved in mineral ion homeostasis.

SYNTHESIS AND METABOLISM:

Vitamin D is synthesised subcutaneously from 7- dehydrocholesterol and is absorbed from intestine , bound to an alpha binding protein in the blood and taken to liver.

In the liver, it is first hydroxylated by the cytochrome oxygenases to **25 hydroxy vitamin D, major storage and circulating form of the hormone.**

In the bound form, it is taken to kidney where again it is hydroxylated by cytochrome **25 hydroxyvitamin D 1 alpha hydroxylase** in the proximal convoluted tubules to 1,25,(OH)2 D. Finally 1,25,(OH)2 D undergoes hydroxylation into inactive metabolites by the enzyme vitamin D 24 hydroxylase.

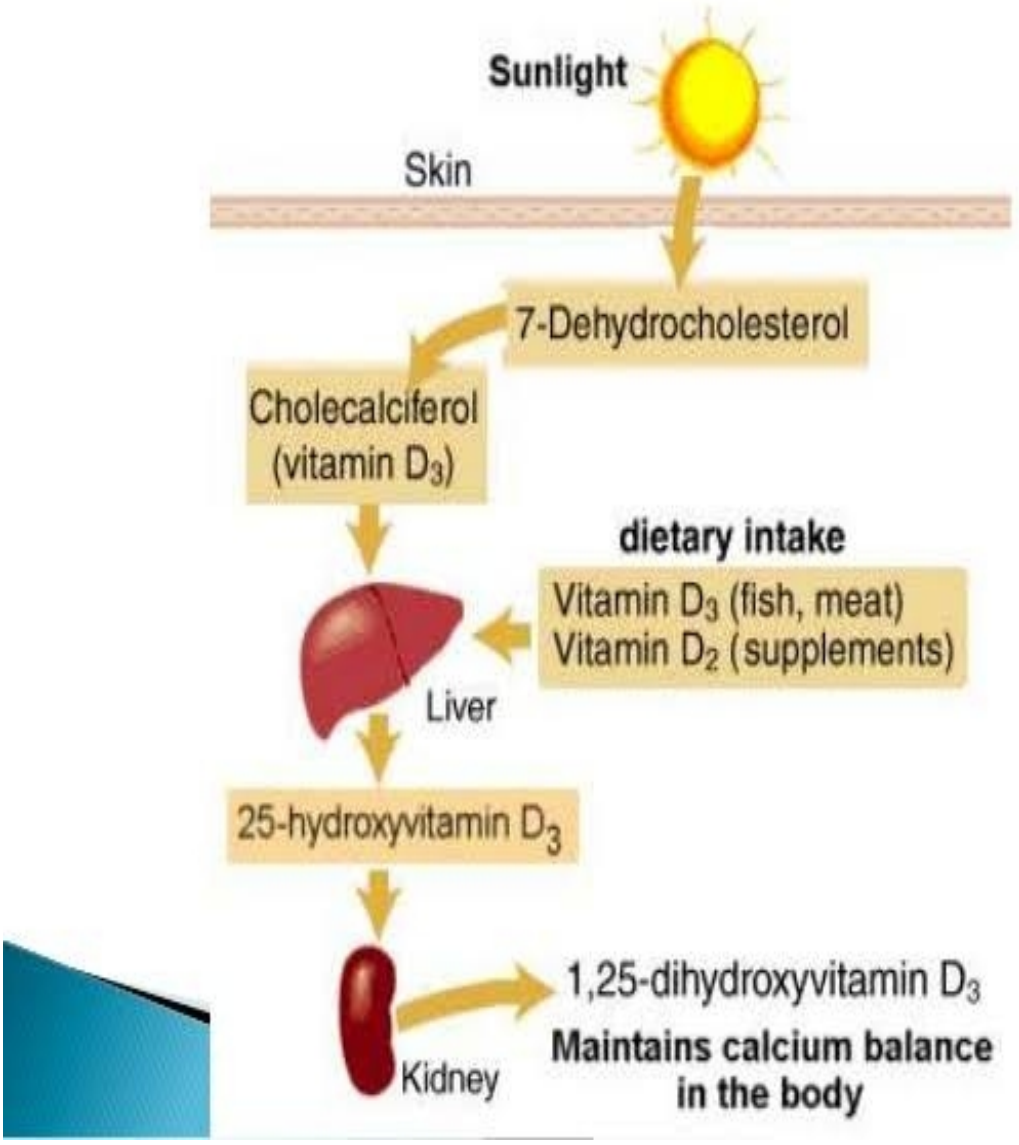


Figure No 4, showing vitamin D synthesis in the body.

Active metablolites of vitamin D that are secreted into bile are reabsorbed by enterohepatic circulation.

PTH and hypophosphatemia are inducers of the enzyme **25 hydroxyvitamin D 1 alpha hydroxylase** whereas calcium , FGF23, 1,25,(OH)2D will suppress it.

SOURCES OF VITAMIN D:

Fortified cereals, diary products, egg yolks, fish oils.

Daily requirement - 600 IU

ACTIONS OF 1,25,(OH)2 D:

It mediates its effect by binding to VITAMIN D RECEPTOR, which is a member of nuclear receptor family.

- **INTESTINE:**
  - It increases the expression of TRPV5 and TRPV6 which are major calcium transporters in the intestine.
  - It stimulates calbindin 9K, calcium binding protein in the intestine, which has a role in the calcium transport along the enterocyte.
- **BONE:**

  Increases resorption of bone by increasing the expression of RANK ligand and stimulating osteoclast activity.

  Increases the expression of bone matrix proteins like osteopontin and osteocalcin and type 1 collagen.

CAUSES OF IMPAIRED VITAMIN D ACTION:

1. VITAMIN D DEFICIENCY:
    - **i.** Defective cutaneous production
    - **ii.** Deficient dietary intake
    - **iii.** Malabsorption
2. INCREASED LOSS OF VITAMIN:
    - **i.** Increased metabolism (phenytoin)
    - **ii.** Enterohepatic circulation impairment
    - **iii.** Nephrotic syndrome
3. IMPAIRED 25 HYDROXYLATION due to liver diseases.
4. IMPAIRED 1 ALPHA HYDROXYLATION:
    - **i.** Hypoparathyroidism
    - **ii.** Renal failure
    - **iii.** 1 alpha hydroxylase mutation
5. END ORGAN RESISTANCE :
    - **i.** VDR mutation
    - **ii.** Phenytoin

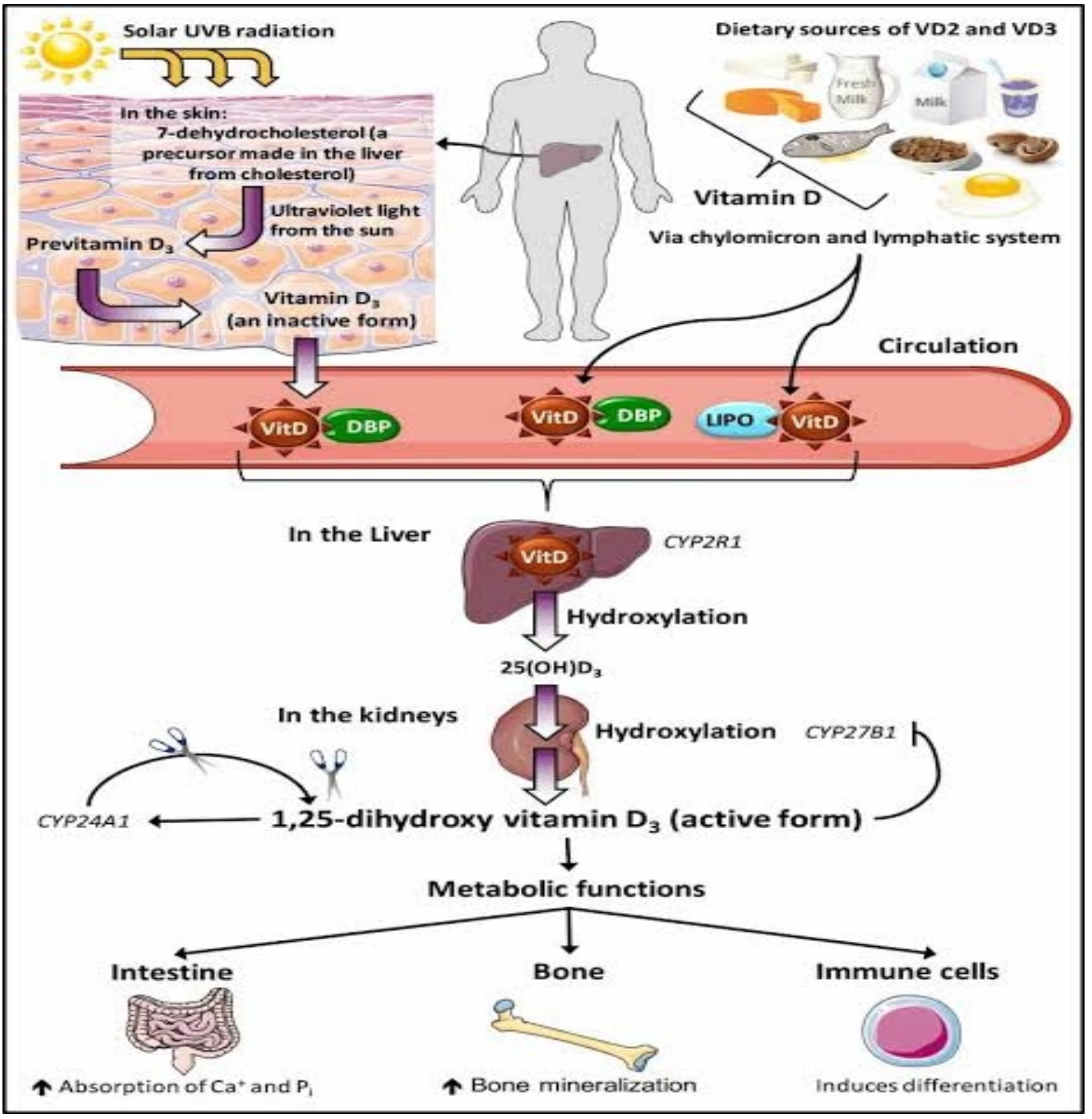


Figure No. 5, Showing Effects Of Vitamin D In Body

CLINICAL MANIFESTATIONS OF VITAMIN D DEFICIENCY:

Manifestations are largely due to defective intestinal calcium absorption. Deficiency for longer duration may cause hypocalcemia , osteomalacia, myopathy.

DIAGNOSIS OF VITAMIN D DEFICIENCY:

Most specific screening test for vitamin D deficiency is serum 25(OH)D level. Levels more than 20 ng/ml is considered adequate.

Metabolic abnormalities:

1. Low calcium (both ionised and total)
2. Low phosphorus
3. Increased PTH.
4. Increased alkaline phosphatase levels due to PTH mediated increased bone turnover.

HYPOCALCEMIA:

Defined as total calcium levels less than 8.5mg/dl with normal serum albumin or ionised calcium less than 4.2 mg/dl.

In the setting of hypoalbuminemia which can falsely lower total calcium levels, corrected calcium levels are measured using the formula given below:

CORRECTED Ca2++ = (Ca++)+[0.8X(4.0-ALBUMIN)]

Figure 5

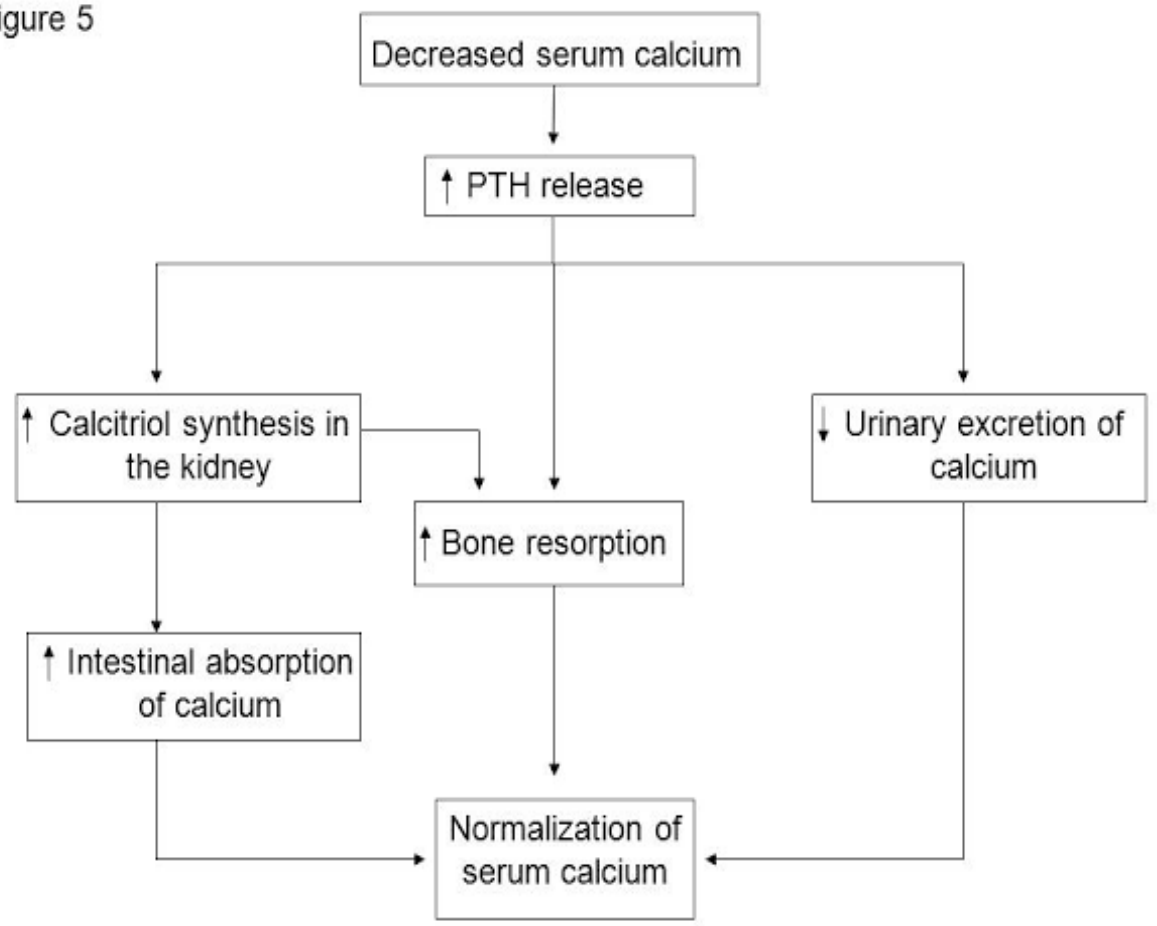


FIG NO: 6 FLOW CHART SHOWING EFFECTS OF LOW CALCIUM AND ITS EFFECTS.

CAUSES OF HYPOCALCEMIA:

Can be due to absent PTH , overproduction or ineffectiveness

LOW PTH LEVELS:

1. Hereditary hypoparathyroidism – due to agenesis
2. Acquired hypoparathyroidism
    i. Surgery
    ii. Radiation
    iii. Infiltration
    iv. Tumor
3. Hypomagnesemia

INEFFECTIVE PTH:

1. Renal disease with impaired production of vitamin D.
2. Nutritional deficiency.
3. Resistance to vitamin D.
4. PTH resistance syndromes including pseudohypoparathyroidism.
5. Altered vitamin D metabolism (phenytoin)

OTHER CAUSES:

1. Acute pancreatitis
2. Tumor lysis syndrome
3. Severe hyperphosphatemia
4. Drugs – bisphosphonates, heparin, protamine sulfate
5. Hungry bone syndrome after parathyroidectomy

CLINICAL MANIFESTATIONS OF HYPOCALCEMIA:

Depends on the degree of hypocalcemia and rate of onset

- Mild and chronic hypocalcemia is usually asymptomatic.
- Acute moderate – leads to circumoral or distal paresthesias and tetany.
- Acute severe - leads to larynospasm, confusion, seizures , vascular collapse with bradycardia and decompensated heart failure.

SIGNS:

TROUSSEAU'S SIGN - inflating the BP cuff 20 mm Hg above SBP for 3 minutes leads to development of carpopedal spasm.

CHVOSTEK SIGN- facial muscle twitching when the nerve is trapped anterior to the ear.

APPROACH AND INVESTIGATIONS:

- History of any systemic diseases and drugs that can cause low calcium levels
- Physical examination for any neck surgery
- Investigations
    i. Serum albumin to rule out hypoalbuminemia
    ii. Serum parathyroid hormone levels
    iii. Serum phosphorus
    iv. 25(OH) vitamin levels
    v. Serum magnesium

MANAGEMENT OF ANTIEPILEPTIC INDUCED BONE LOSS:

Management involves

1. discussing the risk of bone loss and its complications to patients on chronic antiepileptic drugs,
2. to discuss about the risk factors known to aggravate the bone loss and to avoid it
3. to identify high risk patients prior to treatment and evaluate them.

   High risk patients includes

   - Institutionalized And Non-Ambulatory Subjects
   - Increased Duration Of Treatment And Multiple Number Of Drugs
   - Poor Sunlight Exposure
   - Inadequate Dietary Intake
   - Postmenopausal women
   - Hypothyroid patients
   - Smokers and alcoholics
   - Concomitant steroid intake
   - Chronic treatment and increased drugs
4. regular screening for blood biochemical markers and bone density
5. encourage to adopt regular weight bearing exercises, adequate exposure to sunlight and increase the intake of essential nutrients like calcium, phosphorus, vitamin D.

MONITORING:

No clear recommendations have come up for the monitoring of patients with chronic enzyme inducing antiepileptic agents. Suggestions are:

- Monitoring of calcium, phosphorus, vitamin D and PTH before start of the treatment and then at 6 months interval.
- DEXA screening:
- For postmenopausal women on AED's, DEXA is recommended before start of treatment and then at yearly intervals.
- Subjects with one risk factor for osteoporosis should be monitored every 2nd year.
- Subjects with no risk for osteoporosis should be monitored once in 5 years.
- Endocrinologists opinion should be seeked if biochemical parameters are low and DEXA and BMD are low

CALCIUM AND VITAMIN D SUPPLEMENTATION:

The recommended daily requirement of calcium is 400 to 800mg/d and that of vitamin D is 400 IU/D. Patients on antiepileptic therapy should be supplemented with high doses of calcium (1000 to 1500 mg/d) and vitamin D (4000IU/D) because even healthy adults are deficient in vitamin D in India. Studies has been published about the effects of low dose and high dose Vitamin D. After a treatment of one year, BMD is found to be increased and fracture risk has been decreased. In a study conducted by PATICIO et al, fracture has been reduced by 2% in patients on calcium and vitamin D

supplementation. In a study conducted by Krishnamoorthy et al, it has been observed that simultaneous supplementation with calcium and vitamin D has not led to changes in biochemical parameters. Oral bisphosphonates has been tried in preventing osteoporosis.

OBJECTIVES OF THE STUDY

a. To compare and study the levels of calcium and alkaline phosphatase as markers of bone health in patients on antiepileptic therapy and normal patients
b. To assess prevalence of hypocalcemia in patients on antiepileptic therapy.

MATERIALS AND METHODS

STUDY DESIGN - CASE CONTROL STUDY

STUDY PERIOD – October 2017 to August 2018

STUDY POPULATION :

This study was conducted in a outpatient basis in Government Vellore Medical College Hospital among 200 cases who were epileptic patients on antiepileptic drugs and 200 controls who were patients visiting the OP for medical ailments other than epilepsy.

INCLUSION CRITERIA FOR CASES:

1. All epileptic patients of both sexes on antiepileptic therapy
2. Duration of treatment more than 1 year
3. Age – 16 to 50 years

INCLUSION CRITERIA FOR CONTROLS :

1. Non epileptic patients of both sexes.
2. Age – 16 to 50 years

EXCLUSION CRITERIA FOR CASES AND CONTROLS:

1. Patients denying consent
2. Disease known to cause decrease in calcium and increase in alkaline phosphatase levels
3. Drugs causing Hypocalcemia.
4. History of jaundice in the past
5. History of alcohol intake

6. Postmenopausal Women
7. Patients on Calcium And Vitamin D Supplementation
8. Patients with History Of Liver And Renal Diseases
9. Patients on Antitubercular Drugs

DATA COLLECTION :

AFTER obtaining informed consent, detailed history was taken and blood sample taken and sent for investigation and the datas were entered in the proforma designed for the study.

LABORATORY INVESTIGATIONS:

1. SERUM CALCIUM
2. SERUM ALBUMIN
3. RENAL FUNCTION TEST – UREA AND CREATININE
4. SERUM ALKALINE PHOSPHATASE LEVELS
5. SGOT AND SGPT LEVELS

COLLABORATING DEPARTMENTS:

DEPARTMENT OF NEUROLOGY

DEPARTMENT OF BIOCHEMISTRY

EPILEPSY is defined as condition characterised by two or more episodes of unprovoked seizures. The patients started on antiepileptic drugs for the condition are prone to develop metabolic bone disease due to decreased calcium levels due to enzyme inducing properties of the antiepileptic drugs like phenytoin, phenobarbitone, carbamazepine and sodium valproate. Also the levels of serum alkaline phosphatase

levels are increased due to increased bone turnover caused by bone loss. Patients meeting the criteria for study were included. Patients were informed about the study and those accepting to proceed was included after getting informed consent. The presence or absence of the following data was recorded for all the patients in a data extraction proforma –

1. Age and Sex of the patient
2. Occupation
3. History of neck Surgery
4. History of acute abdomen in the past
5. History of radiation in the neck
6. History of jaundice
7. History of alcohol consumption
8. Presence of renal or liver diseases
9. Antitubercular drugs history
10. Hypertension or diabetes mellitus
11. Duration of treatment for epilepsy
12. Type of therapy – Monotherapy Or Dual Therapy Or Triple Therapy
13. Name of the drug taken

History of neck surgery:

History of surgery in the neck especially thyroid surgery or any other neck surgeries are prone to damage the parathyroid gland leading to low parathormone levels and thereby reducing calcium levels in the body.

History of acute abdomen in the past :

Conditions like acute and chronic pancreatitis are known to cause decrease in the calcium levels . Hypocalcemia is one of the component of Ranson Score used for assessing acute pancreatitis. Some possible mechanisms for hypocalcemia are formation of calcium salts, sepsis induced hypocalcemia, hypomagnesaemia induced impaired PTH secretion and action, relative PTH deficiency and vitamin D deficiency

History of radiation to the neck:

As like neck surgery, radiation to the neck for some malignancy may damage the parathyroid gland causing hypocalcemia.

Jaundice in the past:

Obstructive causes of jaundice is known to elevate alkaline phosphatase levels

Alcohol consumption:

Chronic alcoholism leads to hypocalcemia. Possible mechasims include magnesium depletion , impaired PTH release and action, decreased renal tubular absorption of calcium.

Presence of diabetes mellitus:

Diabetes mellitus induced magnesium deficiency can cause hypocalcemia and in cases of diabetic nephropathy hypocalcemia can occur due to reduced synthesis of vitamin D and due to hyperphosphatemia.

Presence of renal and liver diseases:

Presence of renal disease is known to reduce calcium levels by reducing vitamin D synthesis, hyperphosphatemia. Liver disease is known to increase alkaline phosphatase levels and falsely decrease calcium levels due to decrease in serum albumin levels.

Antitubercular drugs:

Drugs like rifampicin are potent enzyme inducers and can cause similar effects like antiepileptic drugs.

Duration of treatment and type of therapy :

Increased duration of treatment and consumption of more than one drug type will increase the severity of hypocalcemia thereby increasing the risk of bone loss and fractures.

Drug taken:

This helps to decide whether antiepileptic drug taken by the patient is an enzyme inducer or non enzyme inducer. Only enzyme inducing drugs can cause abnormalities of bone mineral homeostasis

Drugs causing hypocalcaemia:

1. Heparin
2. Glucagon
3. Protamine sulfate
4. Bisphosphonates
5. Cisplatin

6. Anticonvulsants
7. Aminoglycosides
8. Proton pump inhibitors

After eliciting the details in the proforma, patients blood sample are taken for measuring the levels of calcium, alkaline phosphatase, urea, creatinine, SGOT and SGPT in the blood.

Hypocalcemia is defined as a decrease in total serum calcium level less than 8.5 mg/dl with normal serum albumin levels. Alkaline phosphatase levels more than > 140 IU/L are considered high.

The statistical difference between the biochemical parameters was expressed using **p value , F statistic value , odds ratio and ANOVA.**

Method Of Analysis

Patients age , sex, type of therapy , duration of therapy, serum calcium and alkaline phosphatase levels was calculated. The data was compared with the studies carried out worldwide and in the Indian subcontinent and noted for any differences.

Ethical Issues

1. The objectives and procedure of the study was explained to all patients.
2. Informed consent was taken from all patients willing to participate in the study.
3. The option to opt out of the study was kept open without any clause.
4. Complete confidentiality regarding patient information was maintained through all the stages of the study.

RESULTS

Between 2017 and 2018, 200 cases (patients on antiepileptic therapy) and 200 controls attending outpatient department in department of neurology in Government Vellore Medical College Hospital were studied. Among the 230 cases selected, 30 were excluded from the study. The table below shows the baseline characteristics of the cases and controls included in the study:

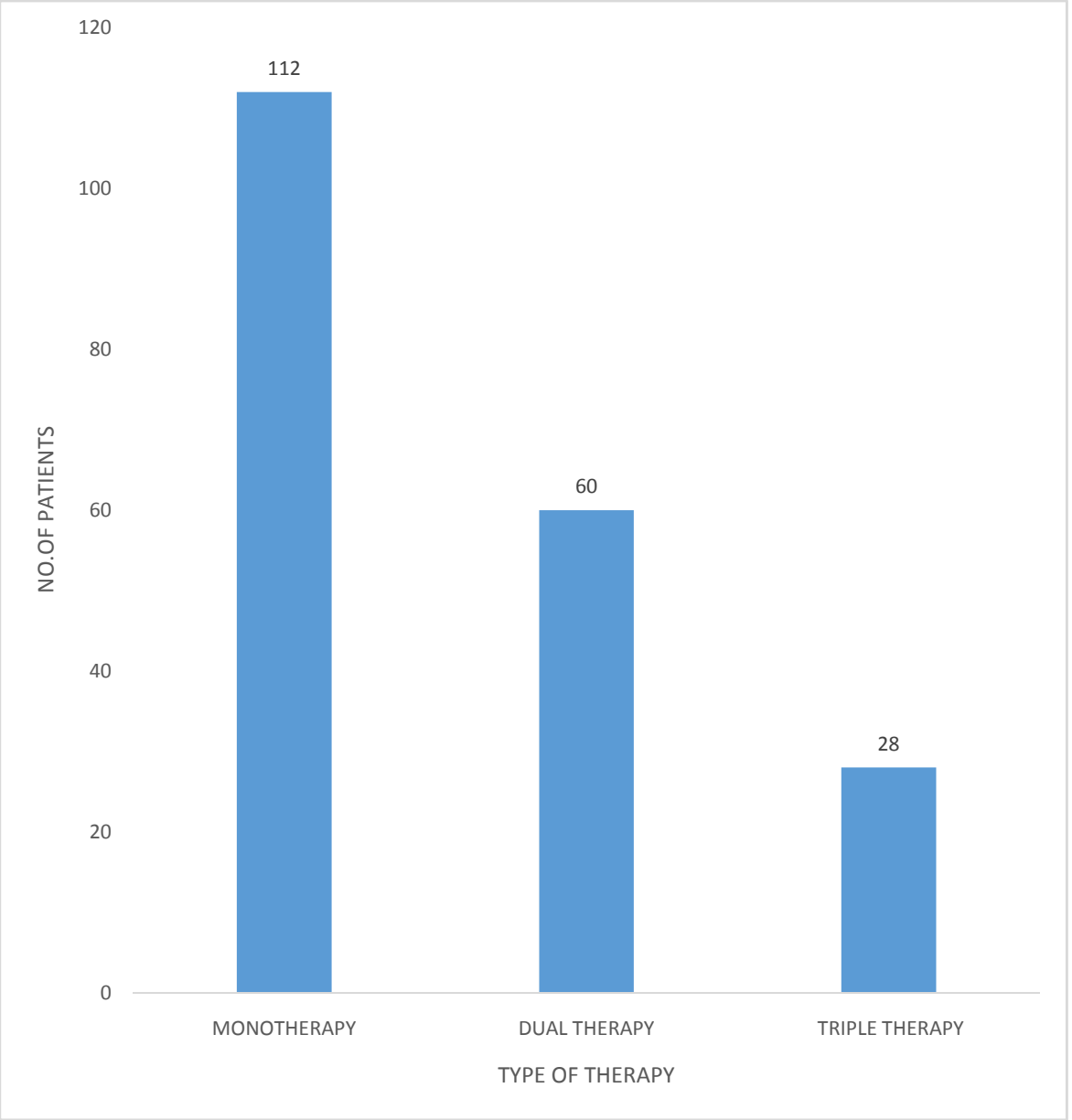
TABLE NO – 2 BASELINE CHARACTERISTICS

CHARACTERISTICS	CASES	CONTROLS
MEAN AGE	31.3 (SD - 9.08)	33.88 (SD - 8.70)
SEX MALE	96 (48%)	101(50.5%)
FEMALE	104(52%)	99(50.5%)

TABLE 3 :BIOCHEMICAL PARAMETERS OF CASES AND CONTROLS

PARAMETERS	CASES	CONTROLS
MEAN ALBUMIN mg/dl	4.59 (SD- 0.19)	4.53 (SD – 0.23)
MEAN UREA mg/dl	23.7 (SD-5.1)	20.5(SD-4.5)
MEAN CREATININE mg/dl	0.75(SD-0.17)	0.73(SD-0.19)
MEAN SGOT IU/L	20.08(SD-3.7)	20.8(SD-5.2)
MEAN SGPT IU/L	24.6(SD-4.4)	26.9(SD-5.6)

FIG NO 7 :FREQUENCY BASED ON TYPE OF THERAPY



Among 200 patients studied, 112 patients were on monotherapy, 60 patients were on dual therapy and 28 patients were on triple therapy.

TABLE NO 4: ANTIEPILEPTIC PROFILE OF PATIENTS

TYPE OF THERAPY	NAME OF THE DRUG	NO OF PATIENTS
MONOTHERAPY	PHENYTOIN	72
	CARBAMAZEPINE	24
	SODIUM VALPROATE	16
DUAL THERAPY	PHENYTOIN + PHENOBARBITONE	13
	PHENYTOIN + CARBAMAZEPINE	21
	PHENYTOIN + SODIUM VALPROATE	18
	CARBAMAZEPINE + SODIUM VALPROATE	8
TRIPLE THERAPY	PHENYTOIN +PHENOBARBITONE+SODIUM VALPROATE	3
	PHENYTOIN+ PHENOBARBITONE +CARBAMAZEPINE	25

TABLE NO : 5 SEX AND CALCIUM LEVELS

	CALCIUM LEVELS	
SEX	**LOW CALCIUM**	**NORMAL CALCIUM**
FEMALE	**56**	**48**
MALE	**48**	**48**

TABLE NO 6 -SEX AND ALKALINE PHOSPHATASE LEVELS

	ALKALINE PHOSPHATASE	
SEX	**HIGH**	**NORMAL**
FEMALE	**60**	**44**
MALE	**59**	**37**

TABLE NO :7 AGE AND CALCIUM LEVELS

	CALCIUM LEVELS	
AGE	**LOW**	**NORMAL**
16 TO 30 YEARS	**37**	**50**
30 TO 55 YEARS	**67**	**46**

TABLE NO: 8 AGE AND ALKALINE PHOSPHATASE LEVELS

	ALKALINE PHOSPHATASE	
AGE	**HIGH**	**NORMAL**
16 TO 30 YEARS	**41**	**46**
30 TO 55 YEARS	**78**	**35**

TABLE NO: 9 COMPARISON OF CALCIUM LEVELS BETWEEN CASES AND CONTROLS

	SERUM CALCIUM	
CASE/CONTROL	**LOWCALCIUM**	**NORMAL**
CASE	97	103
CONTROLS	30	170

The above table compares number of cases and controls with low and normal calcium levels. The observations are that, the patients on antiepileptic therapy are 5.33 times at higher risk of developing hypocalcaemia than the controls with **ODDS RATIO** of **5.33 (3.31 TO 8.5).**

TABLE NO: 10 COMPARISON OF HIGH AND NORMAL ALKALINE PHOSPHATASE LEVELS BETWEEN CASES AND CONTROLS

	ALKALINE PHOSPHATASE	
CASE/ CONTROL	**HIGH**	**NORMAL**
CASES	119	81
CONTROLS	21	179

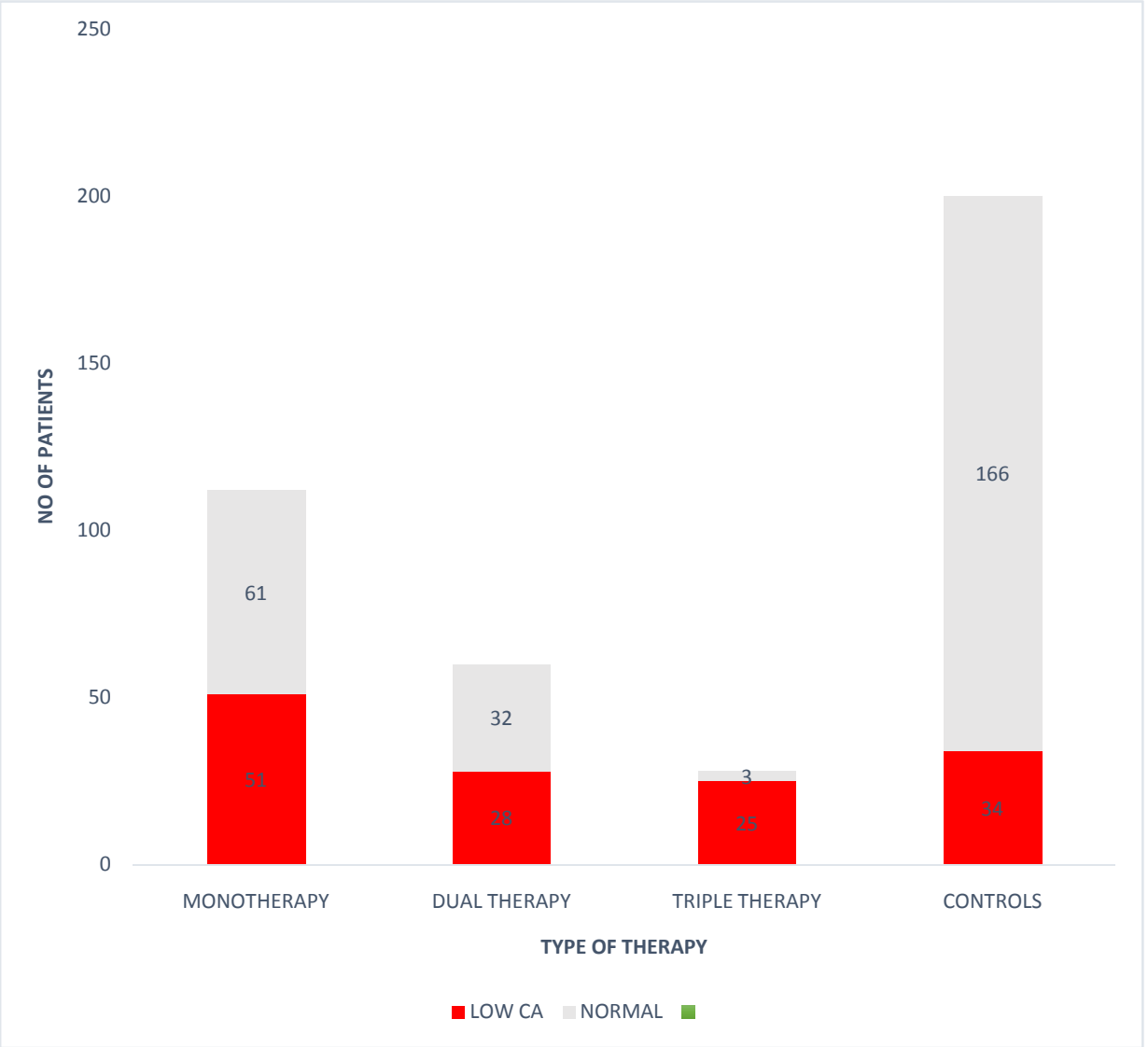
Similar to calcium, the above table compares the high and normal alkaline phosphatase levels between cases and controls. The observations are that the cases are 12.52 times at greater risk of having high alkaline phosphatase levels than the controls with a **ODDS RATIO of 12.52 (7.34 to 21.33). and P value of 0.00**

TABLE NO: 11 MEAN CALCIUM AND ALKALINE PHOSPHATASE VALUES OF CASES AND CONTROLS

CHARACTERISTICS	CASES	CONTROLS
MEAN CALCIUM (mg/dl)	8.22(SD - 0.94)	9.16(SD - 0.66)
MEAN ALKALINE PHOSPHATASE (IU/L)	153.98 (SD - 40.07)	93.09 (SD - 34.15)

The table shows the mean calcium and mean alkaline phosphatase levels of cases and controls. The difference between the two mean calcium values when compared using student t test has a **T value of -11.5 and P value of 0.00** making it statistically significant. The mean alkaline phosphatase value is 153.98 with a **T value of 16.35 and P value of 0.00.**

FIG NO: 8 COMPARISON CHART BETWEEN NO OF CASES AND CONTROLS WITH LOW AND NORMAL CALCIUM VALUES



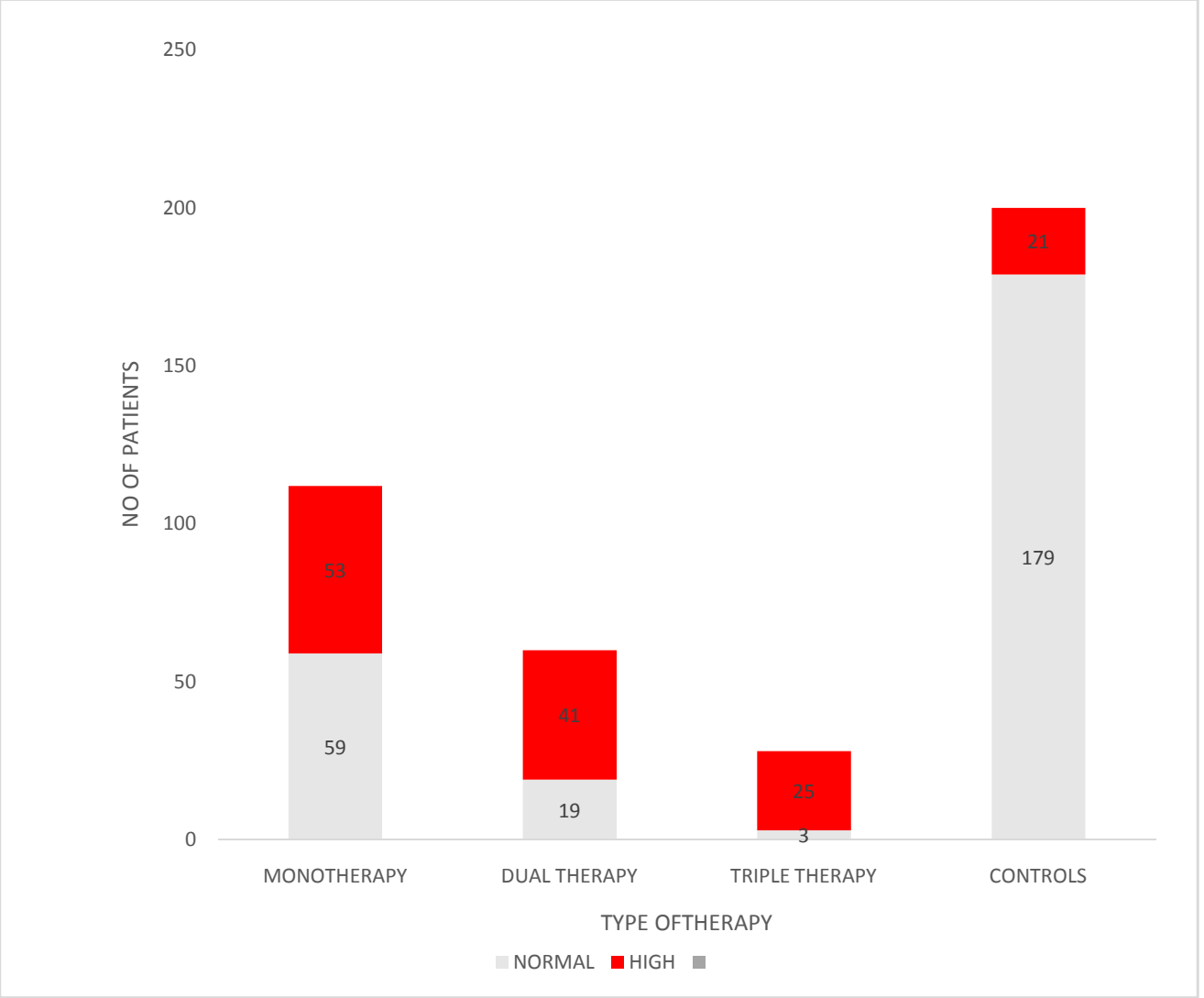
The above chart illustrates the number of patients and controls with low and normal calcium values. Among the patients, based on the type of therapy taken, patients arecompared, with highest number observed among patients taking triple therapy.

TABLE NO: 12 MEAN CALCIUM VALUES OF CASES BASED ON TYPE OF THERAPY

TYPE OF THERAPY	MEAN DURATION OF THERAPY (in years)	MEAN (and SD) CALCIUM VALUES (mg/dl)
MONOTHERAPY	**5.18**	**8.44(0.80)**
DUAL THERAPY	**5.10**	**8.27(0.94)**
TRIPLE THERAPY	**7.87**	**7.23(0.82)**

The above table depicts that the mean calcium values are lowest among patients taking triple therapy and the difference between the three means is statistically significant by **ANOVA (F STATISTIC – 68.7), with a P VALUE OF 0.002**

FIG NO: 9 COMPARISON CHART BETWEEN NO OF CASES AND CONTROLS WITH NORMAL AND HIGH ALKALINE PHOSPHATASE



The above chart depicts the number of patients with normal and high alkaline phosphatase levels. Patients taking different drug types are compared among themselves and among the controls. Highest values are observed among patients taking triple therapy.

TABLE NO: 13 MEAN ALKALINE PHOSPHATASE OF CASES VALUES

BASED ON TYPE OF THERAPY

TYPE OF THERAPY	MEAN DURATION OF THERAPY (in years)	MEAN (SD)ALP VALUES(IU)
MONOTHERAPY	5.18	142.80 (40.2)
DUAL THERAPY	5.10	159.71(35.5)
TRIPLE THERAPY	7.87	186.39(27.4)

The above table describes that high alkaline phosphatase levels are observed among patients taking triple therapyand the difference between the three means is statistically significant by **ANOVA (F STATISTIC –108.46), with a P VALUE OF 0.000**

TABLE NO: 14 ANTIEPILEPTIC DRUGS AND MEAN CALCIUM VALUES

TYPE OF THERAPY	Mean Calcium Values	Std Dev
DUAL THERAPY [PHT+PB]	8.2308	1.1033
DUAL THERAPY[CBZ+SV]	8.5	0.5155
DUAL THERAPY [PHT+CBZ]	7.9952	1.0557
DUAL THERAPY [PHT+SV}	8.5194	0.8148
MONOTHERAPY[CBZ]	8.3167	0.8133
MONOTHERAPY[PHT]	8.4083	0.8297
MONOTHERAPY[SV]	8.8063	0.6148
TRIPLETHERAPY[PHT+PB+CBZ]	7.324	0.8333
TRIPLE THERAPY [PHT+PB+SV]	6.5333	0.3512

FIGURE NO: 10 FREQUENCY BASED ON DURATION OF THERAPY

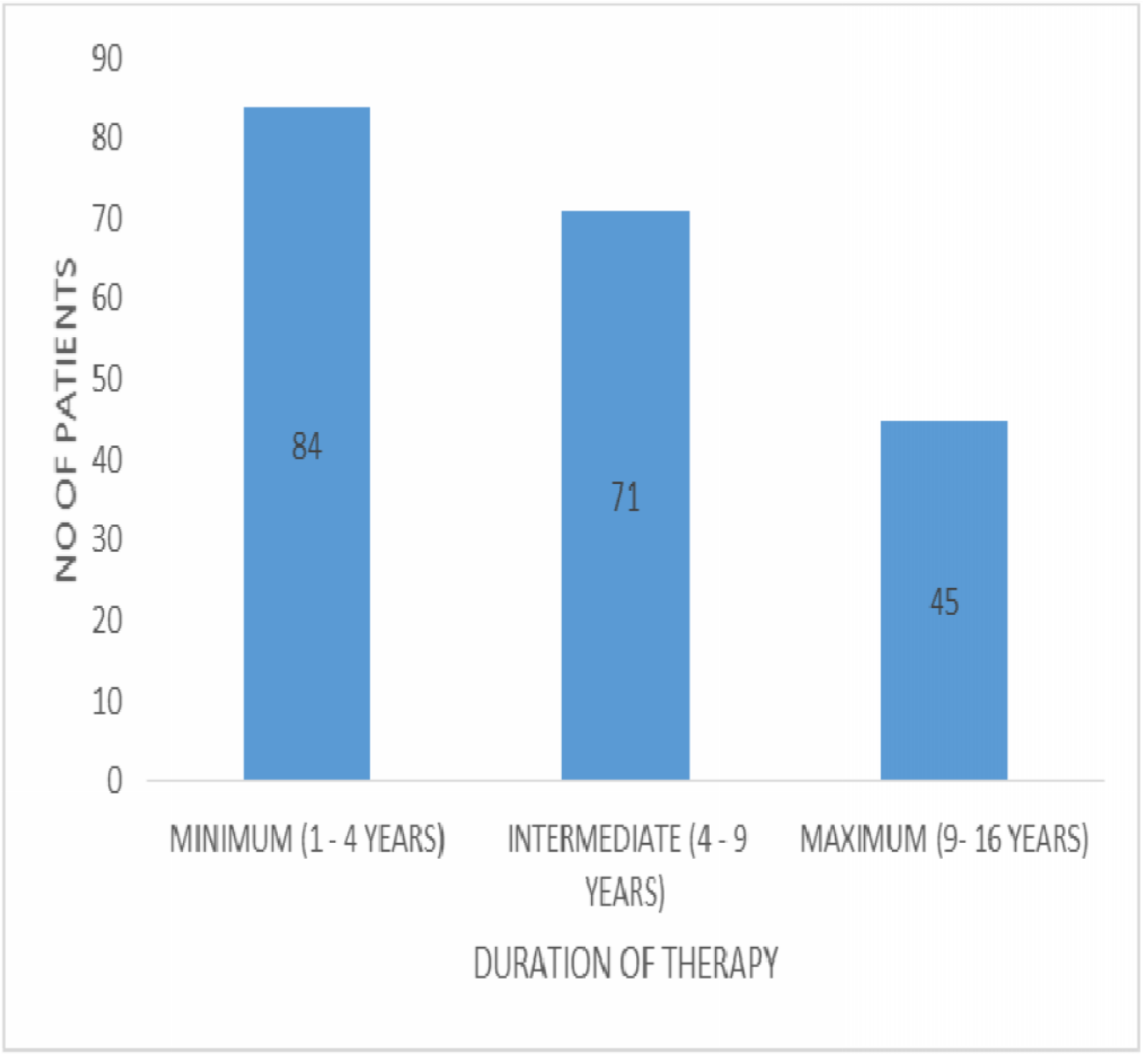
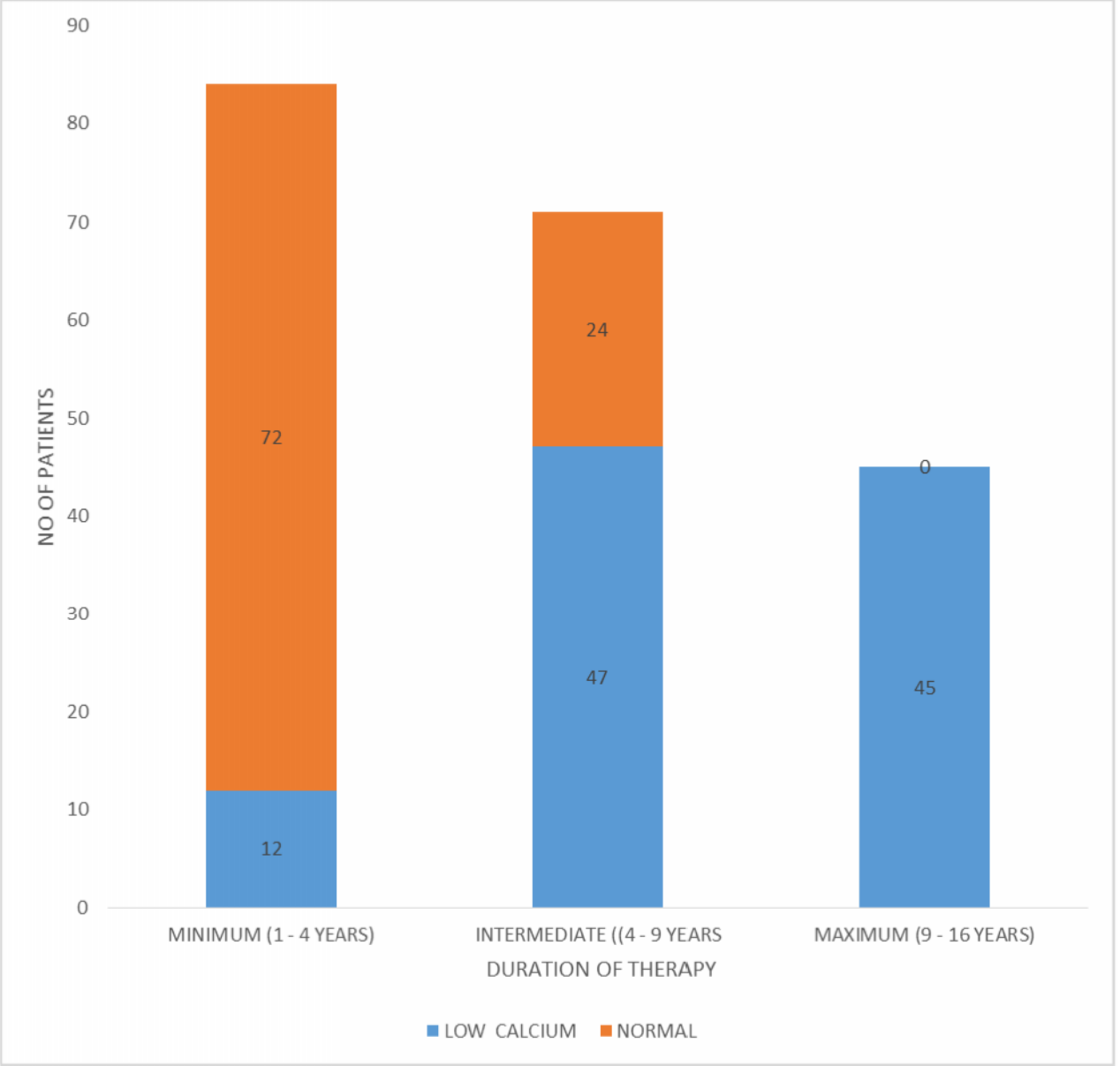
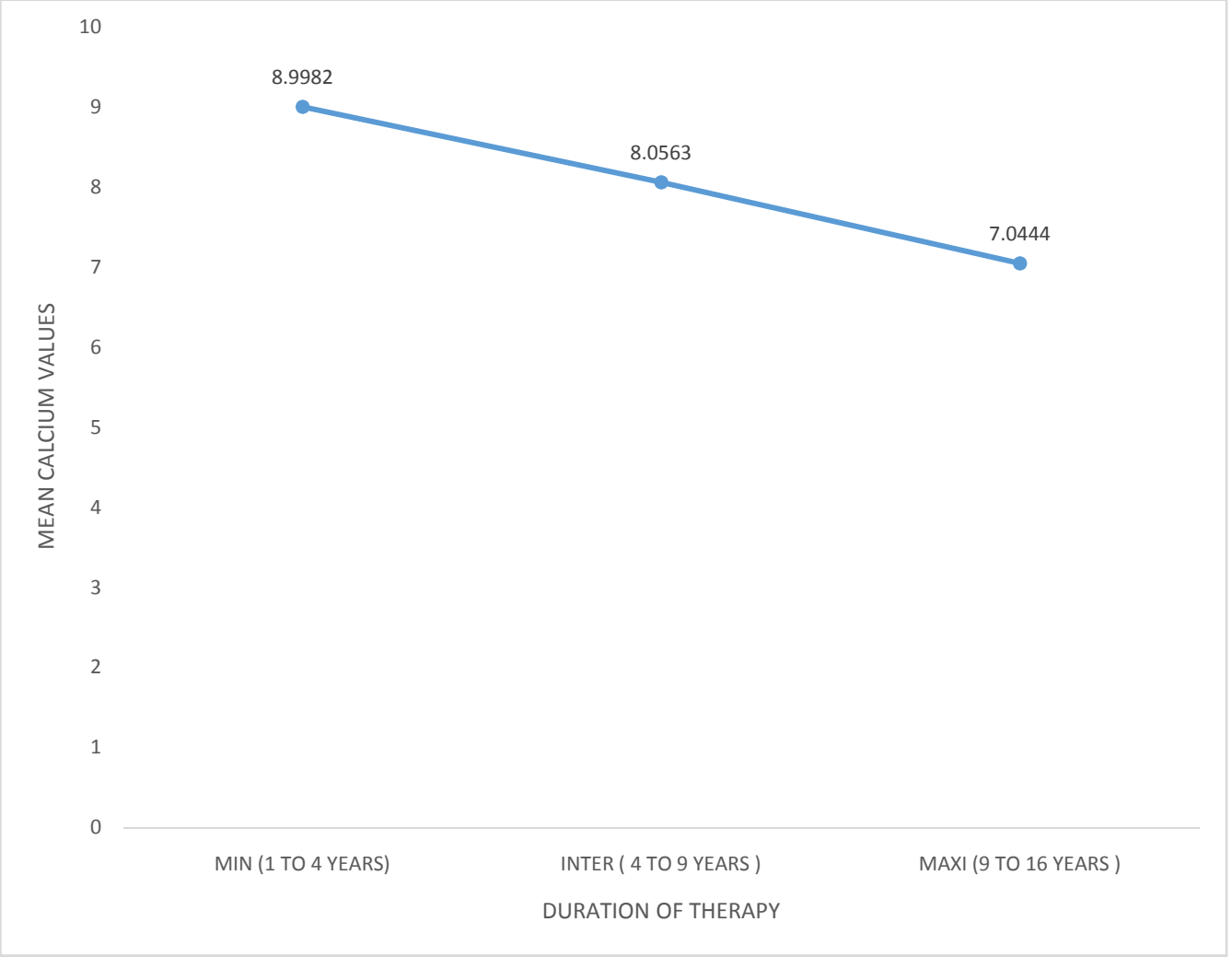


FIGURE NO: 11 COMPARISON CHART BETWEEN NO OF PATIENTS WITH LOW AND NORMAL CALCIUM LEVELS BASED ON DURATION



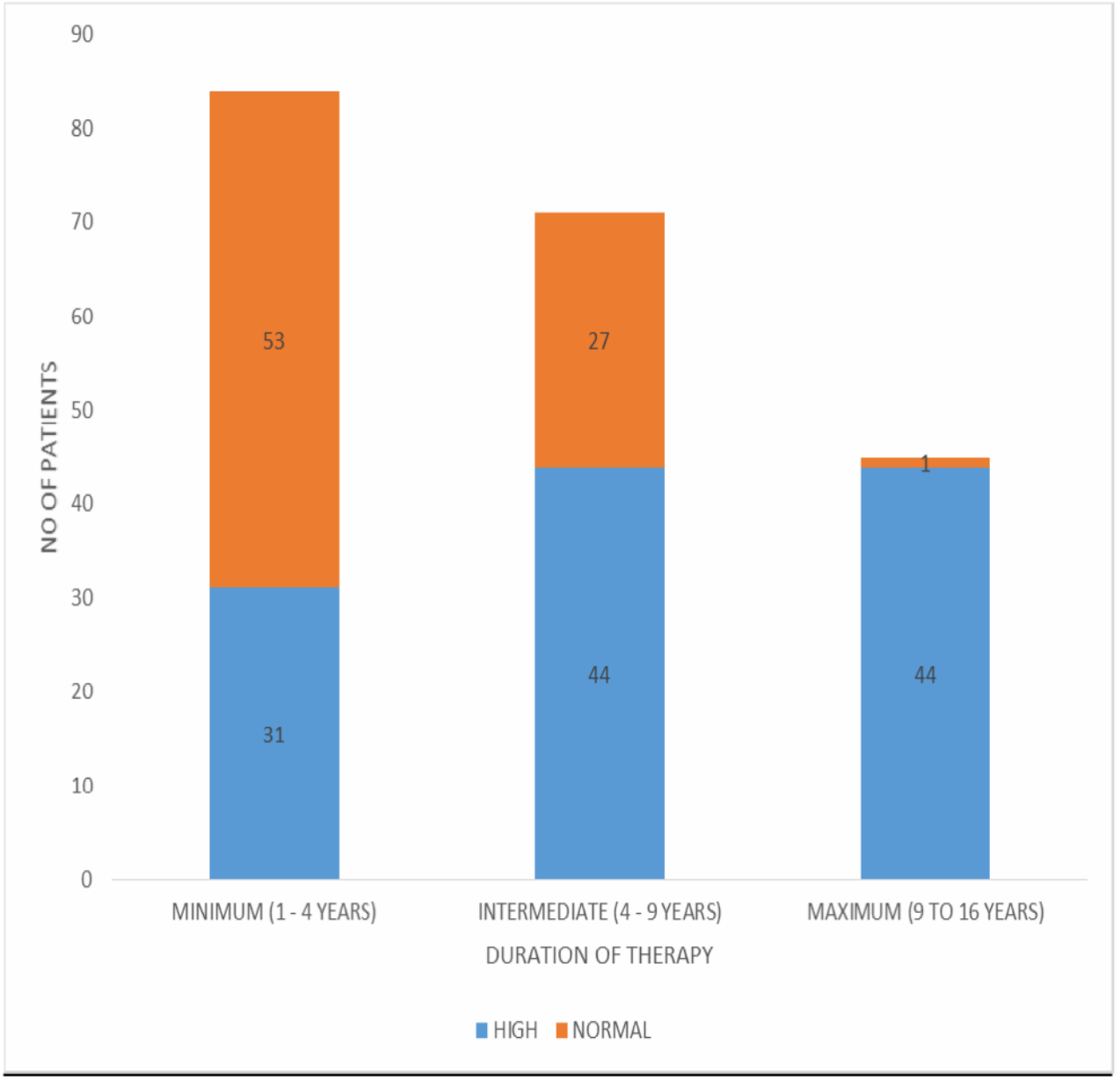
The above chart depicts the number of patients with low and normal calcium values with the duration of therapy.

FIGURE NO: 12 MEAN CALCIUM VALUES BASED ON DURATION OF THERAPY



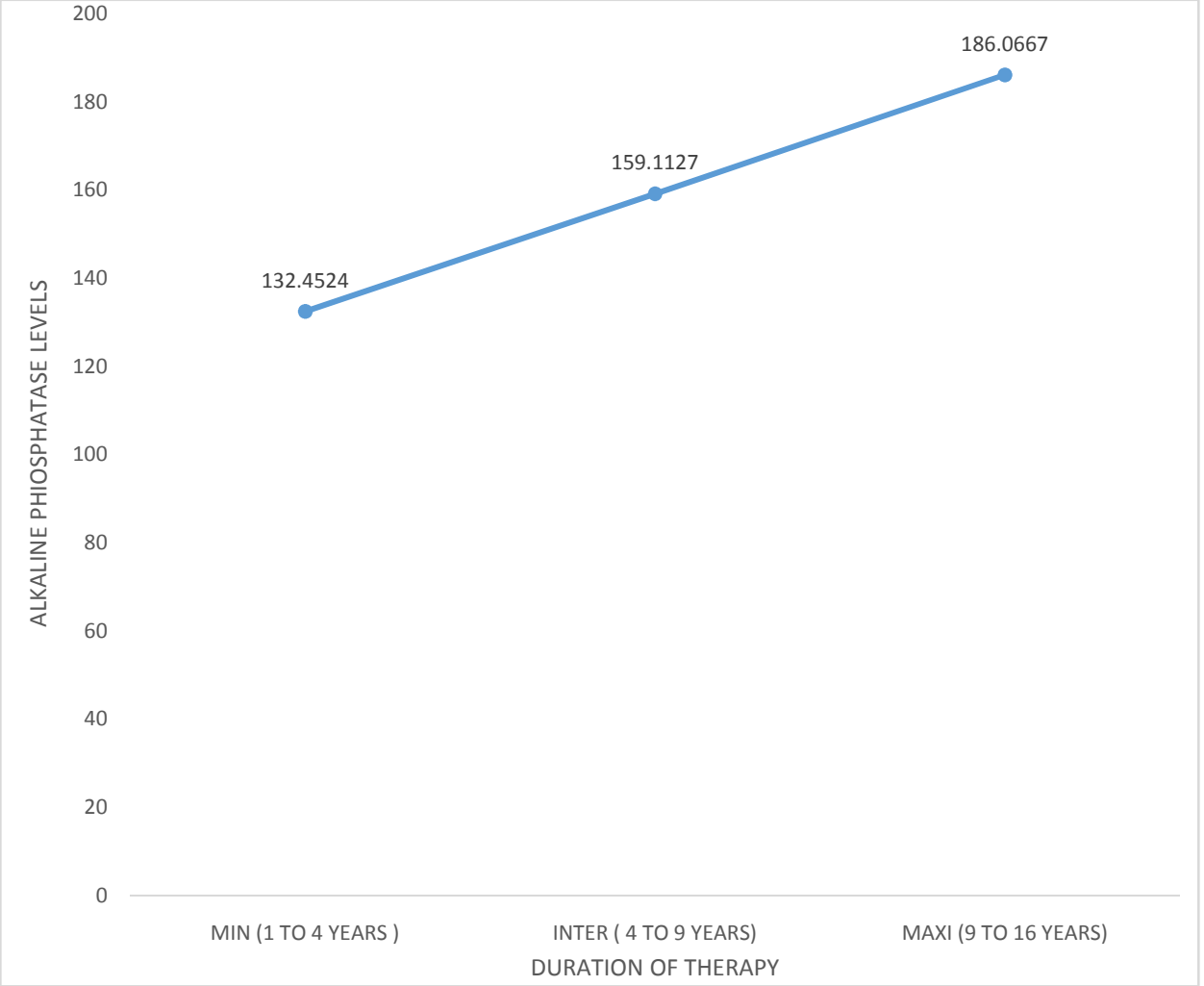
The above chart illustrates that mean calcium value decreases as the duration of therapy increases.There is significant difference between calcium levels in patients on antiepileptic therapy for less than 4 years, more than 4 years and more than 9 years by a ***ANOVA (F STATISTIC – 182.81).***

FIGURE NO: 13 COMPARISON CHART BETWEEN NO OF PATIENTS WITH NORMAL AND HIGH ALKALINE PHOSPHATASE LEVELS BASED ON DURATION



The chart illustrates that among 45 patients taking drugs for 9 to 16 years, 44 were found to have high alkaline phosphatase levels. The inference is that as the duration increases the alkaline phosphatase levels increases among the patients.

FIGURE NO: 14 MEAN ALKALINE PHOSPHATASE VALUES BASED ON DURATION OF THERAPY



The above chart illustrates that the mean alkaline phosphatase values increases as the duration of therapy increases. There is significant difference between calcium levels in patients on antiepileptic therapy for less than 4 years, more than 4 years and more than 9 years by a ***ANOVA (F STATISTIC –36.922).***

DISCUSSION

Epilepsy is a major public health problem worldwide and in India with a prevalence of 50 million and 10 million people affected respectively(2). It predominantly affects people in adolescence and adult age group. Antiepileptics are the main stay of treatment for this disorder. Taking these drugs for a protracted period of time and taking increased number of drugs of different types affects bone mineral metabolism and bone health subclinically , thereby imposing significant risk of fractures which affects the health and quality of life of the patients(8). The minerals commonly affected are calcium, phosphorus, PTH, vitamin D . The levels of these minerals are decreased and hormones like PTH and enzymes like alkaline phosphatase(7,23,27)are increased due to increased bone turnover. The metabolic abnormalities caused by these drugs are less commonly addressed by the treating physicians. Also the patients are not monitored regularly for these abnormalities and are not being supplemented in case of inadequacy. So the levels bone health markers like calcium and alkaline phosphatase in patients on chronic antiepileptic therapy and those not on antiepileptic therapy and whether they need to be started on supplementation or not was analysed in detail in this study.

AGE AND EPILEPSY:

In our study 200 consecutive epileptic patients on antiepileptic therapy and 200 age and gender matched controls were taken for the analysis.

In this study, the mean age of the patients on antiepileptic therapy (cases) and those not on therapy (controls) are**31.3 (SD - 9.08) years** and **33.8 (SD - 8.70)**

years respectively. This closely resembled study done by **RICHENS ROWE ET AL**(15)where the mean age was 36 and 34 for cases and controls respectively.

TABLE NO: 15 shows similar studies showing same age group

S.No	Studies	Mean Age Of Cases And Controls
1.	**Richens Rowe et al**(15)	34 and 36
2.	**Ghafghazi et al**(18)	23 and 25
3.	**Shweta Singla et al**(52)	37.7 and 35.5
4.	**Present Study**	31.3 and 33.8

The importance of age is that most of the patients in our study, are in adult group , the period during which adequate supplementation with minerals will improve their quality of life and thereby reduces the risk of fracture. The table no.7 and 8 depicts that in our study the number of patients with low calcium and high alkaline phosphatase levels are more in the age group of 30 to 55 years.

SEX:

In our study, males and females are in the ratio of 1:1 { Cases – 200 (Males – 96 and Females – 104), Controls- 200 (Males – 101, Females – 99)} . In our study, as depicted in table 5 and 6, the levels of low calcium and high alkaline phosphatase are more in female than in males. A study conducted by Amudhan et al(4) has published that the prevalence of epilepsy in India is more than in males than in females and in other study conducted by MARKOULA et al (53)related to gender specific changes in

BMD in patients on antiepileptic therapy, decrease in BMD is observed more in males than in females. The variation in our study may be due to existing low calcium levels in female population due to poor supplementation, low socioeconomic status.

BIOCHEMICAL PARAMETERS:

The measured biochemical parameters like serum albumin, serum urea and creatinine and serum SGOT and SGPT was not found to have statistically significant difference between the two groups as shown in table 3.

ANTIEPILEPTICS:

All the cases in our study are on treatment with enzyme inducing antiepileptic drugs like phenytoin,phenobarbitone, carbamazepine and sodium valproate for a mean duration of 5.5 years.

Among the 200 cases and 200 controls analysed, **48%** (97 cases) found to have low calcium values and **15%** (30 controls) found to be hypocalcemic. In the study done by **RICHE ROWENS et al**(15)**,** it was observed that 22.5% patients among 160 patients were hypocalcemic.

The mean (+_SD) corrected calcium value of the cases are***8.22 +_0.94mg/dl*** and that of controls are ***9.16 +_0.66 mg/dl.*** The difference between the mean and standard error of differences of corrected calcium of cases and controls is statistically significant with a **P VALUE** of (< 0.05) depicted in table 11. The mean albumin concentration of cases and controls is 4.5mg/dl. The mean(SD) calcium of cases and controls in the study conducted by **RICHE ROWENS et al was 9.25(+_ 0.03)mg/dl**

and 9.73 (+_0.05)mg/dl(15)**.** In another study conducted by **GHAFGHAZI ET AL**the mean calcium of cases and controls was **9.2 (+_0.9)mg/dl**and **10 (+_0.8)mg/dl**(18) respectively. Compared to these studies, the mean calcium of both cases and controls is low in our study which may be due to low dietary calcium intake, poor supplementation due to poor socioeconomic status , high phytate content(54,55) in south Indian diet which inhibits calcium absorption.

Similar to calcium levels, **59.5%** (119 cases) had high alkaline phosphatase levels and 10.5% (21 controls) had high ALP levels. In a study done **GHAFGHAZI ET** (18)**AL, 41%** among 35 patients had increase in alkaline phosphatase levels.

The mean (+_SD) alkaline phosphatase levels of the cases and controls are ***153.98 (+_40.07)IU/L*** and ***93.09 (+_34.15)IU/Lrespectively***. The difference between cases and controls was statistically significant. The observation is that compared to age and gender matched controls, patients on antiepileptic therapy are found to ***have low calcium and high alkaline phosphatase values which is statistically significant with a p value of (<0.05)***

The Table No: 16 depicts different studies showing variations in calcium and ALP levels.

S.NO	STUDIES	% Of Calcium Decreased	% Of ALP Increased
1.	**Richens Rowe et al**(15)	22.5	29
2.	**Shweta Singla et al**(52)	8	-
3.	**Ghafghazi et al**(18)	-	41
4	**Pack et al**(17)	3 to 30	-
5	**Wright**(56)	-	20
6.	**Hunter et al**	30	24
7.	**Present study**	48	59.5

The 200 patients on antiepileptic therapy were subclassified into groups based on duration and type of therapy and within those groups mean calcium and alkaline phosphatase levels were analysed.

Based on duration of therapy:

1. MINIMUM - 1 TO 4 YEARS – 84 PATIENTS
2. INTERMEDIATE – 4 TO 9 YEARS – 71 PATIENTS
3. MAXIMUM – 9 TO 16 YEARS – 45 PATIENTS

The observations are that

1. The mean (+_SD) corrected calcium values are **8.99 (0.51)mg/dl, 8.05(0.68)mg/dl ,7.04 (0.40)mg/dl**in the minimum, intermediate and maximum groups, respectively.
2. The observed alkaline phosphatse levels are **132.4 (37.5)IU/L ,159.1(38.3)IU/L, 186.06(16.8)IU/L** respectively.
3. The results are consistent with the study done by RICHENS ROWE(15) et al, that as the duration of the therapy increases the calcium levels decreases and alkaline phosphatase increases much beyond normal levels. Also the number of patients with low calcium levels and high ALP levels increases as duration increases. This is depicted in the figures 11 to 14.

BASED ON TYPE OF THERAPY:

1. MONOTHERAPY - 112 PATIENTS
2. DUAL THERAPY - 60 PATIENTS
3. TRIPLE THERAPY - 28 PATIENTS

The results are as follows:

1. Mean (+_SD) corrected calcium values are **8.44 (0.80)mg/dl, 8.27 (0.94)mg/dl ,7.23 (0.82mg/dl)** in the three groups respectively.
2. Mean (+_SD) alkaline phosphatase levels are **142.80 (40.2)IU/L ,159.71(35.5)IU/L, 186.39 (27.4)IU/L** respectively.

The findings are similar to the studies conducted by RICHEN ROWE(15) et al, GHAFGHAZI (18)et al and the observations are that compared to monotherapy, patients on triple therapy are found to have significantly lower calcium and higher alkaline phosphatase levels. In a study conducted by RICHENS ROWE et al, the mean calcium of monotherapy, dual therapy and triple therapy was **9.48 (SD+_ 0.12)mg/dl, 9.29 (SD+_0.04)mg/dl and 9.02 (SD+_0.07)mg/dl respectively**. This finding is also low in our study as depicted in figures 8 and 9 and tables 12 and 13.

It is inferred that as the ***duration of therapy and number of drugs increases*** the mean ***calcium and alkaline phosphatase levels decreases and increases*** respectively.

Among the patients taking different types of therapy,

- In monotherapy group, the mean calcium levels are lowest in **carbamazepine group - 8.31 (SD0.8)mg/dl** ,
- In dual therapy it is lowest in***phenytoin and carbamazepine group*** – **7.99 (SD-1.05)mg/dl**
- In triple therapy it is lowest in ***phenytoin, phenobarbitone and sodium valproate group.***

The findings are showed in table 14.

In a study conducted by GHAFGHAZI (18)et al, among dual therapy lower calcium levels were found in patients on phenytoin and phenobarbitone and in triple therapy for patients on PHT, PB and CBZ because sodium valproate was not included in their study.

History of neck surgery, radiation, jaundice and alcohol was found to have no confounding effect on the results obtained.

LIMITATIONS:

- Serum levels of vitamin D, phosphorus and parathyroid hormone and the bone mineral density using DEXA could not be measured due to nonavailability of resources.
- The nutritional status and BMI of the patients was not assessed.
- History of smoking and any thyroid disorders known to have confounding risk was not elicited.

CONCLUSIONS AND RECOMMENDATIONS

Between October 2017 and August 2018, 200 patients on antiepileptic therapy and 200 controls were studied in the outpatient department, in the Department Of Neurology In Government Vellore Medical College Hospital.

- The calcium and alkaline phosphatase levels were analysed in both the groups.
- Compared to controls, patients on antiepileptic therapy found to have low serum calcium and high alkaline phosphatase levels.
- Prevalence of hypocalcemia was found to be 48% among patients on antiepileptic patients.
- Among cases, patients in the age group of 30 to 55 years, found to have lower calcium and high alkaline phosphatase levels compared to that in18 to 30 years.
- Also Females had lower calcium levels compared to males.
- It was also inferred that as the duration of therapy and number of drugs increased, mean calcium and alkaline phosphatase levels is decreased and increased respectively.
- So the physicians treating the patients who are on antiepileptic therapy for chronic duration should give awareness to their patients regarding the possible effects of these drugs on bone mineral metabolism , increased fracture risk and counsel them to avoid intake of factors like alcohol, smoking, steroids and other drugs which can increase the bone loss.

- They should also be counselled to periodically monitor the levels of bone health markers like calcium, phosphorus,vitamin D and alkaline phosphatase in a interval of at least6 months and to be started on adequate supplementation with calcium and vitamin D3 if low levels are detected or if they have multiple risk factors.

They should be advised to have adequate sunlight exposure, to consume diet rich in calcium, vitamin D like diary products, fortified cereals and be started on calcium supplementation around 1000 to 1500 mg/d.

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PROFORMA

NAME :

AGE/SEX :

OP NO :

OCCUPATION :

ADDRESS :

H/O ANY SURGERY IN THE NECK:

H/O ANY ACUTE ABDOMEN IN THE PAST:

H/O ANY RADIATION TO THE NECK IN THE PAST:

PAST H/O JAUNDICE:

COMORBITIES:

SYSTEMIC HYPERTENSION – YES/NO

DIABETES MELLITUS – YES/NO

SEIZURE DISORDER – YES/NO { IF YES – DURATION -

TUBERCULOSIS – YES/NO

KIDNEY DISEASE – YES/ NO

ALCOHOLISM:

DURATION :

AMOUNT CONSUMED PER DAY:

DRUG HISTORY:

ANTIEPILEPTICS-

Phenytoin/Carbmazepine/Phenobarbitone/others

Duration –

MONOTHERAPY / POLYTHERAPY

IF POLYTHERAPY -

- DRUGS FOR OTHER COMORBITIES :

DURATION -

LABORATORY INVESTIGATIONS:

SERUM CALCIUM :

LIVER FUNCTION TEST : ALP –

SGOT-

SGPT-

RENAL FUNCTION TEST :

SERUM ALBUMIN :

CORRECTED CALCIUM VALUE :

MASTER CHART

C / CO	Name	Age	sex	OP No.	Neck Sx	Pst Ac. Abd	RAD	Pst jaundice	HT	DM	SD	Alc	DUR	TYPE OF THERAPY	S.Ca	ALP	S.ALB	Co.ca	urea	Cr	SGOT	SGPT
C	Sathish kumar	36	M	794836	N	N	N	N	N	N	Y	N	2	M[P]	7.9	160	4.3	7.9	36	0.9	26	20
C	Sultan	34	M	867543	N	N	N	N	N	N	Y	N	5	M[P]	7.8	175	4.8	7.8	30	0.7	25	18
C	Dinakaran	32	M	679482	N	N	N	N	N	N	Y	N	1.5	M[P]	8	166	4.7	8	26	0.4	20	18
C	Nagarajan	39	M	828053	N	N	N	N	N	N	Y	N	8	M[P]	7.6	176	4.3	7.6	32	0.6	18	26
C	Vignesh	29	M	816040	N	N	N	N	N	N	Y	N	10	M[P]	7.3	176	4.5	7.3	24	0.8	16	22
C	Kamala	32	F	54028	N	N	N	N	N	N	Y	N	7	M[P]	7.7	196	4.7	7.7	22	0.9	22	18
C	Jayalakshmi	44	F	828209	N	N	N	N	N	N	Y	N	9	M[P]	7.4	172	4.4	7.4	28	0.8	19	22
C	Ellammal	49	F	826450	N	N	N	N	N	N	Y	N	11	M[P]	7.3	194	4.9	7.3	38	0.8	22	26
C	Swetha	10	F	53803	N	N	N	N	N	N	Y	N	10	M[P]	7.4	176	4.3	7.4	22	.0.8	20	24
C	Gopalakrishnan	27	M	827982	N	N	N	N	N	N	Y	N	12	M[P]	7.1	182	4.4	7.1	32	0.8	16	22
C	Pandu rangan	44	M	170160	N	N	N	N	N	N	Y	N	16	M[P]	6.9	184	4.6	6.9	26	0.8	22	26
C	Menaka	30	F	55364	N	N	N	N	N	N	Y	N	10	M[P]	7.3	176	4.4	7.3	22	0.9	22	26
C	Samuel	29	M	825302	N	N	N	N	N	N	Y	N	12	M[P]	7	200	4.9	7	28	0.9	22	26
C	Perumal	18	M	54847	N	N	N	N	N	N	Y	N	8	M[P]	7.5	196	4.3	7.5	22	0.9	22	24

C	Perumal	30	M	54328	N	N	N	N	N	N	Y	N	11	M[P]	7	212	4.6	7	20	0.7	28	13
C	Hemavathy	22	F	82523	N	N	N	N	N	N	Y	N	7	M[P]	7.4	182	4.7	7.4	34	0.8	22	26
C	Bulush	22	F	825435	N	N	N	N	N	N	Y	N	14	M[P]	7.2	188	4.8	7.2	22	0.8	22	24
C	Manjula	27	F	821573	N	N	N	N	N	N	Y	N	9	M[P]	7.7	194	4.9	7.7	22	0.8	18	24
C	Selvaraj	47	M	50178	N	N	N	N	N	N	Y	N	2	M[P]	8.8	56	4.4	8.8	25	1	42	24
C	Samathar	44	F	90954	N	N	N	N	N	N	Y	N	4	M[P]	9.2	100	4.4	9.2	14	1	19	17
C	Devanayagi	40	F	122303	N	N	N	N	N	N	Y	N	6	M[P]	9	102	4.6	9	25	1	16	22
C	Vignesh	18	M	506485	N	N	N	N	N	N	Y	N	2	M[P]	9	114	4.9	9	25	0.9	22	26
C	Vengadabthi	44	M	347013	N	N	N	N	N	N	Y	N	4	M[P]	8.5	122	4.9	8.5	25	0.8	18	22
C	Sasikala	27	F	126782	N	N	N	N	N	N	Y	N	5	M[P]	8.4	136	4.7	8.4	28	0.9	18	24
C	Sekar	46	M	104716	N	N	N	N	N	N	Y	N	3	M[P]	8.8	135	4.6	8.8	26	0.9	18	24
C	Amutha	37	F	435157	N	N	N	N	N	N	Y	N	2	M[P]	10.2	162	4.4	10.2	26	0.7	18	25
C	Perumal	19	M	590069	N	N	N	N	N	N	Y	N	4	M[P]	9.2	142	4.5	9.2	22	0.6	16	22
C	Latha	38	F	182461	N	N	N	N	N	N	Y	N	3	M[P]	9.4	132	4.6	9.4	22	0.7	22	26
C	Kamachi	34	F	441329	N	N	N	N	N	N	Y	N	5	M[P]	9.4	135	4.6	9.4	21	0.9	18	20
C	Ramalingam	39	M	131338	N	N	N	N	N	N	Y	N	3	M[P]	8.7	122	4.6	8.7	18	0.4	18	24
C	Ravi	40	M	585763	N	N	N	N	N	N	Y	N	2.5	M[P]	8.7	110	4.6	8.7	21	0.9	16	22
C	Pooja	20	F	119339	N	N	N	N	N	N	Y	N	4	M[P]	8.6	135	4.7	8.6	18	0.5	18	16
C	Mahesh	20	M	121612	N	N	N	N	N	N	Y	N	2	M[P]	8.7	121	4.7	8.7	22	0.8	12	18
C	Kantha	22	F	594877	N	N	N	N	N	N	Y	N	3	M[P]	8.8	142	4.6	8.8	22	0.9	16	19

C	Kumaresan	24	M	97933	N	N	N	N	N	N	Y	N	2.5	M[P]	9.2	136	4.6	9.2	22	0.7	18	16
C	Chandra	35	F	351413	N	N	N	N	N	N	Y	N	5	M[P]	8.4	150	4.6	8.4	20	0.7	18	22
C	Chandrika	18	F	297267	N	N	N	N	N	N	Y	N	3	M[P]	9	110	4.7	9	19	0.8	16	20
C	Chniraj	46	M	84991	N	N	N	N	N	N	Y	N	3	M[P]	9.2	98	4.8	9.2	20	0.7	16	20
C	Rajeswari	36	F	180611	N	N	N	N	N	N	Y	N	5	M[P]	8.6	112	4.6	8.6	18	0.9	14	18
C	Manjula	40	F	546191	N	N	N	N	N	N	Y	N	2	M[P]	9.6	80	4.6	9.6	18	0.9	14	20
C	Selvarasu	29	M	516328	N	N	N	N	N	N	Y	N	3	M[P]	8.8	110	4.7	8.8	19	0.8	16	20
C	Selvaraj	44	M	810811	N	N	N	N	N	N	Y	N	2	M[P]	9.2	110	4.7	9.2	16	0.9	18	20
C	Dharshini	18	F	151642	N	N	N	N	N	N	Y	N	3	M[P]	9.2	114	4.6	9.2	18	0.9	16	24
C	Vignesh	20	M	51393	N	N	N	N	N	N	Y	N	4	M[P]	8.5	132	4.6	8.5	18	1	16	22
C	Rajendiran	40	M	51478	N	N	N	N	N	N	Y	N	6	M[P]	8.3	130	4.7	8.3	26	0.7	17	14
C	Thamina	20	F	747944	N	N	N	N	N	N	Y	N	3	M[P]	8.6	96	4.8	8.6	22	0.9	14	20
C	Rubini	22	F	815391	N	N	N	N	N	N	Y	N	2	M[P]	8.9	80	4.8	8.9	26	0.8	14	22
C	Subash	20	M	402029	N	N	N	N	N	N	Y	N	5	M[P]	8.4	122	4.6	8.4	22	0.7	18	14
C	Ramakrishnan	45	M	55499	N	N	N	N	N	N	Y	N	3	M[P]	9.4	124	4.7	9.4	20	0.4	16	20
C	Pavithra	18	F	88658	N	N	N	N	N	N	Y	N	4	M[P]	8.8	86	4.7	8.8	28	0.9	20	22
C	Praveen kumar	19	M	808013	N	N	N	N	N	N	Y	N	2	M[P]	9.2	92	4.6	9.2	26	0.5	22	26
C	Venda	28	F	88698	N	N	N	N	N	N	Y	N	5	M[P]	8.3	86	4.4	8.3	18	0.3	20	24
C	Rajalakshmi	19	F	804089	N	N	N	N	N	N	Y	N	2.5	M[P]	9.6	84	4.8	9.6	20	1	21	22
C	Lakshmi	40	F	818702	N	N	N	N	N	N	Y	N	3.5	M[P]	9.1	100	4.2	9.1	18	0.1	26	22

C	Fathima	30	F	173768	N	N	N	N	N	N	Y	N	4.5	M[P]	8.5	92	4.3	8.5	19	0.4	22	24
C	Balaji	44	M	173822	N	N	N	N	N	N	Y	N	2	M[P]	9.8	96	4.4	9.8	26	0.8	16	20
C	Sankar	30	M	173218	N	N	N	N	N	N	Y	N	3.5	M[P]	8.9	104	4.4	8.9	16	0.8	22	26
C	Deepak kumar	19	M	810089	N	N	N	N	N	N	Y	N	5	M[P]	8.6	112	4.6	8.6	34	0.8	23	26
C	Deepan sakra	27	M	438801	N	N	N	N	N	N	Y	N	2.5	M[P]	9.3	95	4.6	9.3	28	0.8	20	24
C	Janani	28	F	812859	N	N	N	N	N	N	Y	N	3.5	M[P]	8.9	98	4.5	8.9	18	0.8	22	26
C	Yukesh	20	M	799367	N	N	N	N	N	N	Y	N	2	M[P]	9.8	96	4.6	9.8	18	0.4	20	24
C	Ganesan	41	M	815596	N	N	N	N	N	N	Y	N	3	M[P]	9.2	100	4.3	9.2	32	0.8	20	26
C	Yasmin	23	F	699734	N	N	N	N	N	N	Y	N	3	M[P]	7.9	180	4.8	7.9	22	0.7	19	22
C	Usha	30	F	407527	N	N	N	N	N	N	Y	N	3	M[P]	7.8	162	4.6	7.8	23	0.9	18	24
C	Anitha	18	F	746767	N	N	N	N	N	N	Y	N	2	M[P]	8.2	130	4.7	8.2	22	0.7	18	25
C	Shakir	18	M	354980	N	N	N	N	N	N	Y	N	2	M[P]	8.1	120	4.6	8.1	28	0.5	22	18
C	Revathy	29	F	654473	N	N	N	N	N	N	Y	N	3	M[P]	7.9	168	4.9	7.9	17	0.4	16	24
C	Ponnarasu	23	M	649425	N	N	N	N	N	N	Y	N	12	M[P]	6.9	176	4.9	6.9	32	0.8	12	24
C	Amutha	37	F	435157	N	N	N	N	N	N	Y	N	10	M[P]	7.3	172	4.7	7.3	28	0.9	18	32
C	Amsa	35	F	342235	N	N	N	N	N	N	Y	N	12	M[P]	6.8	176	4.7	6.8	28	0.4	18	26
C	Perumal	20	M	590069	N	N	N	N	N	N	Y	N	5	M[P]	8	176	4.8	8	26	0.9	25	22
C	Varadhan	55	M	803022	N	N	N	N	N	N	Y	N	2	M[CB]	8	160	4.7	8	34	0.8	20	22
C	Selvi	40	F	376319	N	N	N	N	N	N	Y	N	2	M[CB]	8.1	175	4.8	8.1	22	0.7	22	18
C	Selvam	44	M	139238	N	N	N	N	N	N	Y	N	10	M[CB]	7.8	178	4.7	7.8	22	0.8	19	25

C	Varadhan	25	M	805134	N	N	N	N	N	N	Y	N	8	M[CB]	7.9	186	4.7	7.9	28	0.9	22	25
C	Selvanayagi	23	F	385427	N	N	N	N	N	N	Y	N	9	M[CB]	7.6	192	4.4	7.6	29	0.5	22	24
C	Ranjitha	25	F	129754	N	N	N	N	N	N	Y	N	12	M[CB]	7.2	120	4.5	7.2	28	0.5	21	26
C	Munisami	36	M	129639	N	N	N	N	N	N	Y	N	7	M[CB]	8	156	4.7	8	18	0.4	22	26
C	Ammu	31	F	354836	N	N	N	N	N	N	Y	N	10	M[CB]	7.4	162	4.7	7.4	20	0.8	22	24
C	Selvarani	34	F	218127	N	N	N	N	N	N	Y	N	13	M[CB]	7.3	210	4.8	7.3	19	0.8	18	22
C	Chinnaponnu	36	F	75882	N	N	N	N	N	N	Y	N	11	M[CB]	7.5	177	4.6	7.5	28	0.5	21	25
C	Shankari	34	F	81723	N	N	N	N	N	N	Y	N	9	M[CB]	7.6	196	4.9	7.6	28	0.8	22	26
C	Deivanai	30	F	176201	N	N	N	N	N	N	Y	N	13	M[CB]	7.2	211	4.7	7.2	18	0.3	22	26
C	Karthika	22	F	33609	N	N	N	N	N	N	Y	N	5	M[CB]	8.2	126	4.6	8.2	32	0.9	19	22
C	Priya	19	F	812106	N	N	N	N	N	N	Y	N	2	M[CB]	9.6	98	4.9	9.6	22	0.8	12	16
C	Naveen	22	M	813036	N	N	N	N	N	N	Y	N	3	M[CB]	9.3	112	4.9	9.3	18	0.8	18	24
C	Vasantha	45	F	811134	N	N	N	N	N	N	Y	N	3	M[CB]	9.3	122	4.3	9.3	28	0.6	19	22
C	Ramamoorthy	40	M	810514	N	N	N	N	N	N	Y	N	5	M[CB]	8.4	165	4.6	8.4	18	1	22	28
C	Ezhilarasi	24	F	811135	N	N	N	N	N	N	Y	N	2	M[CB]	9.4	120	4.7	9.4	13	0.5	18	26
C	Jothi	40	F	810842	N	N	N	N	N	N	Y	N	4	M[CB]	8.7	132	4.6	8.7	19	0.8	17	26
C	Janani	20	F	46179	N	N	N	N	N	N	Y	N	2	M[CB]	9.7	118	4.6	9.7	19	0.8	21	26
C	Gowtham raj	21	M	163360	N	N	N	N	N	N	Y	N	4	M[CB]	8.6	98	4.7	8.6	18	0.4	26	21
C	Soundari	28	F	448963	N	N	N	N	N	N	Y	N	3	M[CB]	8.9	102	4.6	8.9	18	0.5	19	24
C	Kalaivani	24	F	50422	N	N	N	N	N	N	Y	N	3	M[CB]	8.5	124	4.7	8.5	20	0.9	18	26

C	Devi	27	F	51833	N	N	N	N	N	N	Y	N	2	M[CB]	9.4	100	4.8	9.4	20	0.9	19	25
C	Kishore	24	M	800821	N	N	N	N	N	N	Y	N	8	M[SV]	7.9	186	4.6	7.9	28	0.9	22	29
C	Kandasamy	45	M	804899	N	N	N	N	N	N	Y	N	10	M[SV]	7.7	186	4.9	7.7	28	0.8	21	26
C	Jayakarthikey	24	M	799781	N	N	N	N	N	N	Y	N	7	M[SV]	8.2	196	4.7	8.2	26	0.9	22	29
C	Gopal	47	M	808185	N	N	N	N	N	N	Y	N	6	M[SV]	8	210	4.5	8	24	0.9	21	26
C	Kamachi	39	F	563298	N	N	N	N	N	N	Y	N	3	M[SV]	8.9	196	4.7	8.9	32	0.8	22	29
C	Gowtham	18	M	808924	N	N	N	N	N	N	Y	N	2	M[SV]	8.9	192	4.6	8.9	22	0.9	16	22
C	Krishnamoorthi	20	M	808930	N	N	N	N	N	N	Y	N	4	M[SV]	8.7	213	4.6	8.7	28	0.7	22	32
C	Selvi	40	F	807998	N	N	N	N	N	N	Y	N	5	M[SV]	8.6	152	4.7	8.6	28	0.5	22	29
C	Saranya	23	F	808484	N	N	N	N	N	N	Y	N	2	M[SV]	9.6	96	4.2	9.6	28	1	22	34
C	Thilagam	42	F	54470	N	N	N	N	N	N	Y	N	2.5	M[SV]	9.6	90	4.3	9.6	28	1	22	26
C	Gomathi	25	F	764243	N	N	N	N	N	N	Y	N	4	M[SV]	9.2	120	4.6	9.2	18	0.8	16	20
C	Selvi	38	M	807991	N	N	N	N	N	N	Y	N	3	M[SV]	9.8	102	4.2	9.8	18	0.5	12	28
C	Murugan	37	M	809163	N	N	N	N	N	N	Y	N	3	M[SV]	9.1	159	4.4	9.1	32	0.6	22	28
C	Darshan	19	M	47193	N	N	N	N	N	N	Y	N	3.5	M[SV]	9	203	4.5	9	22	0.8	21	25
C	Revathi	25	F	306925	N	N	N	N	N	N	Y	N	4	M[SV]	8.8	179	4.9	8.8	22	0.5	22	28
C	Kalpana	26	F	806987	N	N	N	N	N	N	Y	N	2.5	M[SV]	8.9	220	4.7	8.9	22	0.9	22	30
C	Venkatesan	45	M	43670	N	N	N	N	N	N	Y	N	8	D[CB+SV]	7.6	204	4.6	7.6	22	0.7	22	26
C	Priya	18	F	791397	N	N	N	N	N	N	Y	N	4	D[CB+SV]	8.3	132	4.7	8.3	28	0.8	26	39
C	Jayamary	47	F	795300	N	N	N	N	N	N	Y	N	3	D[CB+SV]	8.6	196	4.7	8.6	28	0.9	18	26

C	Venkatesan	40	M	795102	N	N	N	N	N	N	Y	N	3	D[CB+SV]	8.8	182	4.7	8.8	32	0.7	22	28
C	Pooja	19	F	796123	N	N	N	N	N	N	Y	N	2.5	D[CB+SV]	9	179	4.6	9	28	0.5	21	25
C	Padma	40	F	797244	N	N	N	N	N	N	Y	N	3.5	D[CB+SV]	8.4	169	4.9	8.4	18	0.7	22	29
C	Santhosh	21	M	797257	N	N	N	N	N	N	Y	N	5	D[CB+SV]	8.1	136	4.7	8.1	17	0.8	22	29
C	Ramakrishnan	25	M	79748	N	N	N	N	N	N	Y	N	2	D[CB+SV]	9.2	126	4.6	9.2	18	0.5	18	20
C	Mohankumar	35	M	78941	N	N	N	N	N	N	Y	N	3	D [P+SV}	7.9	166	3.8	7.95	28	0.4	22	18
C	Lakshmi	40	F	742009	N	N	N	N	N	N	Y	N	9	D [P+SV}	7.6	180	4.6	7.6	28	0.6	22	32
C	Vijayalakshmi	29	F	47890	N	N	N	N	N	N	Y	N	6	D [P+SV}	7.9	162	4.6	7.9	28	0.9	18	24
C	Sudha	25	F	46000	N	N	N	N	N	N	Y	N	8	D [P+SV}	7.5	195	4.6	7.5	22	0.8	22	32
C	Kamal basha	45	M	794935	N	N	N	N	N	N	Y	N	12	D [P+SV}	6.8	200	4.6	6.8	28	0.9	22	26
C	Damotharan	34	M	794701	N	N	N	N	N	N	Y	N	10	D [P+SV}	7.3	159	4.3	7.3	28	0.9	22	30
C	Sandhiya	17	F	672932	N	N	N	N	N	N	Y	N	2	D [P+SV}	9.2	120	4.2	9.2	22	0.9	20	26
C	Lathamaheshwari	30	F	291372	N	N	N	N	N	N	Y	N	4	D [P+SV}	8.7	110	4.3	8.7	18	0.6	20	24
C	Sekar raj	40	M	233625	N	N	N	N	N	N	Y	N	3.5	D [P+SV}	8.9	86	4.6	8.9	22	0.9	18	20
C	Sandhiya	20	F	672932	N	N	N	N	N	N	Y	N	4	D [P+SV}	8.5	136	4.3	8.5	22	0.9	22	28
C	Deepa	24	F	41983	N	N	N	N	N	N	Y	N	2	D [P+SV}	9.3	186	4.3	9.3	28	0.4	20	24
C	Thirupathy	23	M	44063	N	N	N	N	N	N	Y	N	3	D [P+SV}	9.3	178	4.4	9.3	22	0.7	22	26
C	Velu	40	M	384381	N	N	N	N	N	N	Y	N	3.5	D [P+SV}	9	164	4.5	9	28	0.6	22	29
C	Nazema	30	F	490096	N	N	N	N	N	N	Y	N	2	D [P+SV}	9.6	172	4.5	9.6	19	0.8	22	36
C	Murali	35	M	792725	N	N	N	N	N	N	Y	N	2.5	D [P+SV}	9.3	132	4.5	9.3	20	0.9	22	28

C	Saravanan	39	M	43600	N	N	N	N	N	N	Y	N	3	D [P+SV}	8.9	128	4.3	8.9	32	0.9	22	29
C	Vinoth	28	M	798893	N	N	N	N	N	N	Y	N	4	D [P+SV}	8.6	104	4.2	8.6	18	0.8	22	29
C	Siva	22	M	825682	N	N	N	N	N	N	Y	N	3	D [P+SV}	9	98	4.3	9	28	0.9	21	19
C	Nadhiya	31	F	346050	N	N	N	N	N	N	Y	N	10	D [P+C]	6.6	190	3.9	6.7	24	0.4	21	25
C	Megala	32	F	645234	N	N	N	N	N	N	Y	N	5	D [P+C]	7.6	182	4.8	7.6	22	0.9	19	25
C	Mohankumar	33	M	217894	N	N	N	N	N	N	Y	N	4	D [P+C]	7.8	185	4.7	7.8	22	0.4	22	24
C	Kamachi	34	F	441329	N	N	N	N	N	N	Y	N	6	D [P+C]	6.9	220	4.7	6.9	28	0.9	19	26
C	Megaladevi	35	F	734123	N	N	N	N	N	N	Y	N	6	D [P+C]	7.5	166	4.6	7.5	22	0.8	22	30
C	Monikaselvi	32	M	336563	N	N	N	N	N	N	Y	N	9	D [P+C]	6.8	198	4.6	6.8	18	0.6	20	26
C	Sultana	36	M	635732	N	N	N	N	N	N	Y	N	12	D [P+C]	6.4	192	4.6	6.4	19	0.8	18	20
C	Murugan	45	M	768420	N	N	N	N	N	N	Y	N	8	D [P+C]	7.5	206	4.6	7.5	18	0.8	18	24
C	Umapathi	40	M	797330	N	N	N	N	N	N	Y	N	11	D [P+C]	6.6	183	4.8	6.6	19	0.8	22	26
C	Meenakshi	31	F	785583	N	N	N	N	N	N	Y	N	7	D [P+C]	7.6	186	4.6	7.6	19	0.8	20	25
C	Sathish	19	M	799670	N	N	N	N	N	N	Y	N	3	D [P+C]	9.2	176	4.6	9.2	17	0.7	20	25
C	Nirmal kumar	24	M	772018	N	N	N	N	N	N	Y	N	4	D [P+C]	8.8	198	4.4	8.8	18	0.8	18	24
C	Subramani	38	M	797898	N	N	N	N	N	N	Y	N	3.5	D [P+C]	8.9	204	4.2	8.9	18	0.8	19	25
C	Rani	30	F	797828	N	N	N	N	N	N	Y	N	7	D [P+C]	7.5	132	4.7	7.5	22	0.8	22	36
C	Kanishka	18	F	997783	N	N	N	N	N	N	Y	N	2	D [P+C]	9.3	112	4.6	9.3	20	0.7	22	26
C	Meena	30	F	798156	N	N	N	N	N	N	Y	N	8.5	D [P+C]	7.2	193	4.8	7.2	20	0.7	21	28
C	Murugendiran	36	M	797631	N	N	N	N	N	N	Y	N	3.5	D [P+C]	9	152	4.7	9	20	0.6	28	19

C	Vikram	18	M	797959	N	N	N	N	N	N	Y	N	1.5	D [P+C]	9.8	110	4.6	9.8	18	0.9	28	33
C	Saravanan	33	M	796021	N	N	N	N	N	N	Y	N	4.5	D [P+C]	8.6	118	4.3	8.6	19	0.5	22	30
C	Poongodhai	39	F	150289	N	N	N	N	N	N	Y	N	3	D [P+C]	9.3	98	4.7	9.3	20	0.8	12	22
C	Devagi	36	F	800855	N	N	N	N	N	N	Y	N	3.5	D [P+C]	8.9	126	4.8	8.9	20	0.9	18	24
C	Lalitha	35	F	62471	N	N	N	N	N	N	Y	N	8	D [P+PB]	8	166	4.6	8	22	0.8	20	18
C	Raja	25	M	128292	N	N	N	N	N	N	Y	N	6	D [P+PB]	7.4	180	4.8	7.4	21	0.9	21	25
C	Rukmani	43	F	791799	N	N	N	N	N	N	Y	N	7	D [P+PB]	6.9	178	4.6	6.9	18	0.9	21	32
C	Murali	32	M	791601	N	N	N	N	N	N	Y	N	10	D [P+PB]	6.5	195	4.6	6.5	20	0.7	18	22
C	Yuvaraj	25	M	790276	N	N	N	N	N	N	Y	N	3	D [P+PB]	8.9	163	4.6	8.9	28	0.9	21	32
C	Shilpa	23	F	54689	N	N	N	N	N	N	Y	N	7	D [P+PB]	7.2	169	4.5	7.2	22	0.7	22	38
C	Velan	40	M	803012	N	N	N	N	N	N	Y	N	9	D [P+PB]	7.1	159	4.6	7.1	20	0.8	21	26
C	Nandhini	19	F	802559	N	N	N	N	N	N	Y	N	4	D [P+PB]	8.9	162	4.9	8.9	28	0.8	22	38
C	Monika	21	F	796089	N	N	N	N	N	N	Y	N	2	D [P+PB]	9.6	82	4.7	9.6	20	0.8	21	29
C	Abdul	36	M	803469	N	N	N	N	N	N	Y	N	3.5	D [P+PB]	8.9	172	4.3	8.9	20	0.5	18	20
C	Chithra	39	F	55826	N	N	N	N	N	N	Y	N	1.5	D [P+PB]	9.8	82	4.6	9.8	22	0.9	16	20
C	Lakshmi narasimhan	43	M	46409	N	N	N	N	N	N	Y	N	2.5	D [P+PB]	9.2	152	4.7	9.2	20	0.8	21	16
C	Sekar	36	M	807023	N	N	N	N	N	N	Y	N	5	D [P+PB]	8.6	196	4.3	8.6	18	0.5	20	16
C	Anandhi	34	F	116840	N	N	N	N	N	N	Y	N	12	TRI [P+PB+CB	6.9	175	4.6	6.9	32	0.8	19	22

C	Thayar	26	F	353374	N	N	N	N	N	N	Y	N	8	TRI [P+PB+CB	6.3	196	4.8	6.3	32	0.5	18	25
C	Sekar	43	M	104716	N	N	N	N	N	N	Y	N	6	TRI [P+PB+CB	6.3	184	4.7	6.3	32	0.9	24	28
C	Latha	34	F	182461	N	N	N	N	N	N	Y	N	6	TRI [P+PB+CB	6.6	200	4.4	6.6	32	0.9	16	22
C	Kalaivani	24	F	50422	N	N	N	N	N	N	Y	N	8	TRI [P+PB+CB	7.2	215	4.6	7.2	32	0.8	12	24
C	Devi	32	F	51823	N	N	N	N	N	N	Y	N	11	TRI [P+PB+CB	7	196	4.9	7	28	0.2	18	26
C	Jayasri	28	F	50736	N	N	N	N	N	N	Y	N	6	TRI [P+PB+CB	7.6	192	4.6	7.6	26	0.9	18	26
C	Rajasekar	40	M	50831	N	N	N	N	N	N	Y	N	10	TRI [P+PB+CB	7	186	4.5	7	32	0.8	22	28
C	Yasodha	37	F	52033	N	N	N	N	N	N	Y	N	9	TRI [P+PB+CB	7.2	192	4.4	7.2	32	0.8	18	26
C	Raziya	39	F	815091	N	N	N	N	N	N	Y	N	12	TRI [P+PB+CB	6.5	200	4.2	6.5	32	0.7	22	26
C	Suresh	28	M	44958	N	N	N	N	N	N	Y	N	7	TRI [P+PB+CB	7.3	210	4.6	7.3	32	0.7	22	28

C	Ramesh	32	M	63080	N	N	N	N	N	N	Y	N	8	TRI [P+PB+CB	7.2	198	4.8	7.2	28	0.7	16	20
C	Monika	19	F	804019	N	N	N	N	N	N	Y	N	5	TRI [P+PB+CB	7.6	210	4.5	7.6	28	0.7	18	25
C	Kandasamy	45	M	80499	N	N	N	N	N	N	Y	N	13	TRI [P+PB+CB	6.8	182	4.7	6.8	28	0.5	41	29
C	Ramu	49	M	132768	N	N	N	N	N	N	Y	N	9	TRI [P+PB+CB	6.7	210	4.6	6.7	25	0.9	23	32
C	Lalitha	37	F	184173	N	N	N	N	N	N	Y	N	11	TRI [P+PB+CB	6.3	198	4.8	6.3	32	0.9	22	29
C	Thilaga	36	F	464282	N	N	N	N	N	N	Y	N	10	TRI [P+PB+CB	6.8	212	4.8	6.8	32	0.9	22	26
C	Sasi	32	M	217893	N	N	N	N	N	N	Y	N	11	TRI [P+PB+CB	6.5	199	4.6	6.5	20	1	22	32
C	Revathi	29	F	803956	N	N	N	N	N	N	Y	N	5	TRI [P+PB+CB	7.8	198	4.7	7.8	19	0.9	22	30
C	Kalpana	28	F	806987	N	N	N	N	N	N	Y	N	3	TRI [P+PB+CB	8.4	189	4.7	8.4	28	0.9	22	26
C	Pongodi	32	F	790924	N	N	N	N	N	N	Y	N	4	TRI [P+PB+CB	8.3	166	4.9	8.3	32	0.9	19	28

C	Ramar	45	M	32149	N	N	N	N	N	N	Y	N	2	TRI [P+PB+CB	9	206	4.3	9	22	0.9	22	29
C	Sumathi	43	F	393825	N	N	N	N	N	N	Y	N	3	TRI [P+PB+CB	8.8	110	4.3	8.8	28	0.8	22	26
C	Mubarak	22	F	52434	N	N	N	N	N	N	Y	N	3	TRI [P+PB+CB	8.6	118	4.8	8.6	20	0.5	20	26
C	Pandiyan	46	M	671289	N	N	N	N	N	N	Y	N	4.5	TRI [P+PB+CB	8.4	120	4.6	8.4	22	0.9	21	26
C	Anandh	34	M	225739	N	N	N	N	N	N	Y	N	12	TRI[P+PB +SV]	6.5	189	4.8	6.5	22	0.9	22	16
C	Rajesh	37	M	252869	N	N	N	N	N	N	Y	N	9	TRI[P+PB +SV]	6.9	176	4.7	6.9	18	1	22	32
C	Latha selvi	42	F	204629	N	N	N	N	N	N	Y	N	13	TRI[P+PB +SV]	6.2	192	4.9	6.2	32	0.9	11	25
C	Santhoshwaran	22	M	615428	N	N	N	N	N	N	N	N	4	M[P]	8.3	78	4.5	8.3	20	0.5	18	23
CO	Jayasri	24	F	50724	N	N	N	N	N	N	N	N	-	-	9.9	46	4.3	9.9	24	0.5	22	43
CO	Loganathan	19	M	817211	N	N	N	N	N	N	N	N	-	-	9.8	88	4.3	9.8	18	0.5	17	28
CO	Kalaiarasi	40	F	817170	N	N	N	N	N	N	N	N	-	-	10.2	96	4.5	10.2	22	0.9	22	42
CO	Boopalan	36	M	31691	N	N	N	N	N	N	N	N	-	-	8.9	48	4.1	8.9	17	0.4	17	21
CO	Mahalakshmi	20	F	165315	N	N	N	N	N	N	N	N	-	-	8.7	107	4.6	8.7	28	1	26	30

CO	Vasantha	40	F	163652	N	N	N	N	N	N	N	N	-	-	9.9	71	4.3	9.9	20	0.9	22	30
CO	Mohan	36	M	632723	N	N	N	N	N	N	N	N	-	-	9.6	68	4.1	9.6	18	0.7	19	26
CO	Sajithabegam	23	F	191236	N	N	N	N	N	N	N	N	-	-	9.3	55	4	9.3	16	0.5	16	22
CO	Prasanth	29	M	51629	N	N	N	N	N	N	N	N	-	-	9.8	112	4.5	9.8	16	0.8	18	36
CO	Malar	40	F	818692	N	N	N	N	N	N	N	N	-	-	9.1	78	4.8	9.1	19	0.4	18	32
CO	Prabakaran	42	M	923661	N	N	N	N	N	N	N	N	-	-	9.1	38	4.4	9.1	20	0.4	18	23
CO	Chakkaravarthi	40	M	747621	N	N	N	N	N	N	N	N	-	-	10.3	105	4.9	10.3	24	0.6	32	36
CO	Kuppusamy	45	M	645671	N	N	N	N	N	N	N	N	-	-	8.6	63	4.2	8.6	17	0.8	20	28
CO	Priyalakshmi	21	F	931645	N	N	N	N	N	N	N	N	-	-	8.9	76	4.4	8.9	21	0.5	23	34
CO	Lokesh	18	M	456210	N	N	N	N	N	N	N	N	-	-	9.4	89	4.8	9.4	24	1.1	26	32
CO	Gopi	25	M	931647	N	N	N	N	N	N	N	N	-	-	9.7	92	4.6	9.7	20	1	29	31
CO	Kanaka	48	F	52526	N	N	N	N	N	N	N	N	-	-	8.7	52	4.3	8.7	18	0.5	18	29
CO	Venda	27	F	51484	N	N	N	N	N	N	N	N	-	-	9.6	82	4.3	9.6	18	0.6	16	28
CO	Yasotha	36	F	801179	N	N	N	N	N	N	N	N	-	-	9.8	112	4.7	9.8	18	0.8	22	29
CO	Elango	43	M	78372	N	N	N	N	N	N	N	N	-	-	9.3	92	4.9	9.3	22	0.5	18	32
CO	Renuka	39	F	788716	N	N	N	N	N	N	N	N	-	-	8.9	76	4.2	8.9	17	0.8	18	32
CO	Balaji	22	M	821438	N	N	N	N	N	N	N	N	-	-	9.6	92	4.9	9.6	28	0.8	22	28
CO	Ramakrishnan	42	M	81775	N	N	N	N	N	N	N	N	-	-	9.8	86	4.8	9.8	18	0.9	18	20
CO	Abdulla	45	M	51751	N	N	N	N	N	N	N	N	-	-	8.8	99	4.9	8.8	19	0.6	20	32
CO	Parithra	20	F	822393	N	N	N	N	N	N	N	N	-	-	9.8	102	4.3	9.8	17	0.4	18	26

CO	Mohan	18	M	817595	N	N	N	N	N	N	N	N	-	-	9.3	82	4.5	9.3	19	0.8	16	26
CO	Lakshmi	43	F	826204	N	N	N	N	N	N	N	N	-	-	9.3	132	4.4	9.3	18	0.8	16	20
CO	Dhanam	36	F	55423	N	N	N	N	N	N	N	N	-	-	8.8	112	4.4	8.8	18	0.9	18	25
CO	Tamilselvi	25	F	54845	N	N	N	N	N	N	N	N	-	-	8.7	122	4.3	8.7	18	0.8	18	26
CO	Babu	25	M	824859	N	N	N	N	N	N	N	N	-	-	9.1	104	4.3	9.1	19	0.5	22	28
CO	Bajo	48	M	826198	N	N	N	N	N	N	N	N	-	-	9.7	112	4.6	9.7	18	0.4	17	22
CO	Shanmugam	32	M	55525	N	N	N	N	N	N	N	N	-	-	9.3	98	4.2	9.3	18	0.7	46	14
CO	Marsaiyyam	46	M	55096	N	N	N	N	N	N	N	N	-	-	8.8	112	4.2	8.8	28	1	38	24
CO	Pandu rayan	45	M	82982	N	N	N	N	N	N	N	N	-	-	9.7	49	4.2	9.7	35	1.2	24	20
CO	Sethu	42	M	82963	N	N	N	N	N	N	N	N	-	-	8.9	72	4.3	8.9	18	0.8	14	23
CO	Kamala	38	F	131647	N	N	N	N	N	N	N	N	-	-	9.7	97	4.7	9.7	24	1.2	28	18
CO	Subba	32	M	133762	N	N	N	N	N	N	N	N	-	-	9.4	84	4.5	9.4	22	1	25	32
CO	Bhuranesh	22	M	50590	N	N	N	N	N	N	N	N	-	-	10.8	27	5	10.8	15	0.3	32	28
CO	Vinoth	23	M	566499	N	N	N	N	N	N	N	N	-	-	9	96	4.6	9	33	0.8	23	28
CO	Hariprasanth	27	M	56655	N	N	N	N	N	N	N	N	-	-	9.2	112	4.3	9.2	18	0.9	18	28
CO	Ramesh	36	M	53579	N	N	N	N	N	N	N	N	-	-	9	42	4.6	9	18	0.6	18	26
CO	Imthiyash	43	M	53892	N	N	N	N	N	N	N	N	-	-	9.2	56	4.3	9.2	18	0.5	12	32
CO	Mithuna	30	F	816443	N	N	N	N	N	N	N	N	-	-	9.3	43	4.6	9.3	18	0.6	18	26
CO	Balaraman	37	M	931662	N	N	N	N	N	N	N	N	-	-	9.4	42	4.2	9.4	23	0.7	22	28
CO	Chithra	28	F	916387	N	N	N	N	N	N	N	N	-	-	9.8	136	4.4	9.8	21	0.9	21	29

CO	Aruna	20	F	316593	N	N	N	N	N	N	N	N	-	-	8.8	81	4.7	8.8	25	0.6	23	31
CO	Samuel	27	M	643081	N	N	N	N	N	N	N	N	-	-	9.5	123	4.6	9.5	19	1	18	25
CO	Sundari	40	F	913470	N	N	N	N	N	N	N	N	-	-	10	110	4.9	10	26	1.4	31	21
CO	Saroja	46	F	931636	N	N	N	N	N	N	N	N	-	-	9.9	94	4.2	9.9	22	0.8	22	26
CO	Babu	23	M	346558	N	N	N	N	N	N	N	N	-	-	9.7	81	4	9.7	18	0.6	18	22
CO	Babu	27	M	824859	N	N	N	N	N	N	N	N	-	-	9.8	32	4.7	9.8	19	0.4	18	26
CO	Kanniyammal	46	F	770891	N	N	N	N	N	N	N	N	-	-	9.2	62	4.3	9.2	17	0.8	18	29
CO	Dhanush	19	M	82806	N	N	N	N	N	N	N	N	-	-	9.6	20	4.3	9.6	18	0.7	18	26
CO	Durga	32	F	858080	N	N	N	N	N	N	N	N	-	-	9.3	82	4.3	9.3	17	0.5	18	26
CO	Aswin	23	M	828101	N	N	N	N	N	N	N	N	-	-	8.9	46	4.5	8.9	20	1	18	29
CO	Subramani	40	M	826556	N	N	N	N	N	N	N	N	-	-	9.7	112	4.3	9.7	18	0.7	22	38
CO	Jaya	36	F	827219	N	N	N	N	N	N	N	N	-	-	8.9	98	4.5	8.9	19	0.6	16	28
CO	Roja	20	F	827848	N	N	N	N	N	N	N	N	-	-	8.8	78	4.3	8.8	17	0.5	18	28
CO	Valli	36	F	53957	N	N	N	N	N	N	N	N	-	-	10.3	122	4.7	10.3	20	0.9	18	27
CO	Saravanan	35	M	821634	N	N	N	N	N	N	N	N	-	-	9.6	88	4.8	9.6	22	0.5	12	28
CO	Balaraman	46	M	801918	N	N	N	N	N	N	N	N	-	-	8.9	92	4.7	8.9	17	0.6	22	38
CO	Radha	40	F	15699	N	N	N	N	N	N	N	N	-	-	9.8	62	4.8	9.8	20	0.6	18	32
CO	Fathima	20	F	818771	N	N	N	N	N	N	N	N	-	-	9.6	56	4.2	9.6	28	0.5	22	28
CO	Mariyammal	40	F	52921	N	N	N	N	N	N	N	N	-	-	9.3	72	4.3	9.3	18	0.5	18	29
CO	Malar	40	F	759275	N	N	N	N	N	N	N	N	-	-	8.9	92	4.8	8.9	18	0.8	22	28

CO	Divya	19	F	817179	N	N	N	N	N	N	N	N	-	-	9.8	66	4.9	9.8	17	0.8	19	26
CO	Manigandan	36	M	818843	N	N	N	N	N	N	N	N	-	-	9.8	98	4.6	9.8	18	0.7	17	26
CO	Subasri	32	F	659381	N	N	N	N	N	N	N	N	-	-	9.9	67	4.8	9.9	32	1.1	19	24
CO	Gopal	40	M	732681	N	N	N	N	N	N	N	N	-	-	9	118	4.8	9	17	0.6	22	28
CO	Komathy	35	F	820025	N	N	N	N	N	N	N	N	-	-	8.9	42	4.8	8.9	16	0.8	19	32
CO	Krishnan	45	M	821734	N	N	N	N	N	N	N	N	-	-	9.3	36	4.3	9.3	17	0.6	16	28
CO	Muthu	45	M	824184	N	N	N	N	N	N	N	N	-	-	8.6	56	4.3	8.6	17	0.9	28	37
CO	Seetha	27	F	822312	N	N	N	N	N	N	N	N	-	-	9.3	46	4.7	9.3	18	0.9	22	16
CO	Santhosh	19	M	51648	N	N	N	N	N	N	N	N	-	-	10.2	96	4.3	10.2	18	0.5	26	18
CO	Suriya	19	F	171232	N	N	N	N	N	N	N	N	-	-	9.3	82	4.3	9.3	25	0.6	46	32
CO	Rani	40	F	812205	N	N	N	N	N	N	N	N	-	-	8.8	118	4.5	8.8	24	0.9	23	35
CO	Chandirasekar	36	M	808728	N	N	N	N	N	N	N	N	-	-	9.8	82	4.2	9.8	19	0.9	12	18
CO	Raman	40	M	791196	N	N	N	N	N	N	N	N	-	-	9.4	92	4.4	9.4	18	0.7	22	36
CO	Perameshwari	45	F	710200	N	N	N	N	N	N	N	N	-	-	9.2	110	4.4	9.2	17	0.4	32	18
CO	Yasotha	34	F	162488	N	N	N	N	N	N	N	N	-	-	8.9	128	4.8	8.9	16	0.4	22	36
CO	Vatchala	43	F	804834	N	N	N	N	N	N	N	N	-	-	10.3	84	4.9	10.3	22	0.5	18	26
CO	Purusothaman	20	M	815054	N	N	N	N	N	N	N	N	-	-	9.9	86	4.3	9.9	25	0.8	22	36
CO	Sumathi	38	F	806112	N	N	N	N	N	N	N	N	-	-	9.5	86	4.3	9.5	18	0.5	12	28
CO	Ranganathan	46	M	1327636	N	N	N	N	N	N	N	N	-	-	8.9	88	4.7	8.9	29	1.1	29	28
CO	Jaya	32	F	191315	N	N	N	N	N	N	N	N	-	-	10.3	75	4.5	10.3	27	0.4	30	24

CO	Jaruth	24	M	131614	N	N	N	N	N	N	N	N	-	-	9	62	4.2	9	25	0.6	27	20
CO	Pounammal	45	F	16738	N	N	N	N	N	N	N	N	-	-	9.5	88	4.6	9.5	28	0.9	17	29
CO	Sarath	23	M	46551	N	N	N	N	N	N	N	N	-	-	9.6	82	4.6	9.6	22	0.9	12	18
CO	Renuga	38	F	803849	N	N	N	N	N	N	N	N	-	-	9.8	90	4.6	9.8	20	0.8	21	30
CO	Alazal khan	27	M	808129	N	N	N	N	N	N	N	N	-	-	9	97	4.6	9	18	0.9	13	25
CO	Sumathi	38	F	880611	N	N	N	N	N	N	N	N	-	-	8.9	100	4.3	8.9	18	0.7	21	28
CO	Purushothmam	20	M	815054	N	N	N	N	N	N	N	N	-	-	8.9	98	4.6	8.9	18	0.8	16	20
CO	Uma	36	F	162488	N	N	N	N	N	N	N	N	-	-	9.3	100	4.7	9.3	18	0.9	16	18
CO	Parameshwari	40	F	710200	N	N	N	N	N	N	N	N	-	-	9.8	102	4.7	9.8	18	0.8	16	22
CO	Chandrasekar	36	M	791196	N	N	N	N	N	N	N	N	-	-	8.8	98	4.8	8.8	32	0.9	21	26
CO	Suresh	32	M	720916	N	N	N	N	N	N	N	N	-	-	9.6	88	4.7	9.6	18	0.9	21	26
CO	Kala	32	F	679011	N	N	N	N	N	N	N	N	-	-	10.2	100	4.6	10.2	18	0.7	21	25
CO	Najaraj	36	F	889250	N	N	N	N	N	N	N	N	-	-	9.8	92	4.6	9.8	18	0.8	18	20
CO	Perumal	40	M	6397	N	N	N	N	N	N	N	N	-	-	9.3	40	4.7	9.3	18	0.9	21	27
CO	Jayanthi	19	F	931655	N	N	N	N	N	N	N	N	-	-	9.5	78	4.9	9.5	29	0.9	23	30
CO	Rani	36	F	583044	N	N	N	N	N	N	N	N	-	-	9.3	65	4.7	9.3	24	0.7	21	27
CO	Sankari	38	F	602505	N	N	N	N	N	N	N	N	-	-	9.7	57	4.5	9.7	28	0.8	25	32
CO	Manimegalai	42	F	191931	N	N	N	N	N	N	N	N	-	-	9.1	52	4.4	9.1	20	0.5	19	24
CO	Venda	27	F	764007	N	N	N	N	N	N	N	N	-	-	9.2	72	4.3	9.2	18	0.9	21	27
CO	Yasotha	36	F	801179	N	N	N	N	N	N	N	N	-	-	8.9	92	4.7	8.9	18	0.8	21	26

CO	Elangovan	43	M	783172	N	N	N	N	N	N	N	N	-	-	8.8	120	4.6	8.8	32	0.9	18	12
CO	Renuka	34	F	788716	N	N	N	N	N	N	N	N	-	-	9.2	86	4.8	9.2	32	0.7	21	28
CO	Prasanth	30	M	51629	N	N	N	N	N	N	N	N	-	-	9.3	62	4.7	9.3	28	0.9	16	18
CO	Malar	40	F	818692	N	N	N	N	N	N	N	N	-	-	8.9	92	4.9	8.9	19	0.8	20	26
CO	Loganathan	20	M	817211	N	N	N	N	N	N	N	N	-	-	8.8	100	4.6	8.8	22	0.9	22	36
CO	Jayasri	24	F	50726	N	N	N	N	N	N	N	N	-	-	10.3	96	4.6	10.3	32	0.8	20	26
CO	Kalairani	25	F	50422	N	N	N	N	N	N	N	N	-	-	9.3	98	4.6	9.3	32	0.9	22	28
CO	Rajendiran	45	M	51478	N	N	N	N	N	N	N	N	-	-	9.6	102	4.3	9.6	28	0.8	20	24
CO	Rani	40	F	812205	N	N	N	N	N	N	N	N	-	-	9.6	90	4.6	9.6	18	0.3	18	22
CO	Elumalai	38	M	802990	N	N	N	N	N	N	N	N	-	-	8.6	98	4.6	8.6	18	0.9	22	26
CO	Mohan	35	F	35048	N	N	N	N	N	N	N	N	-	-	8.9	112	4.6	8.9	28	0.8	22	28
CO	Vijaya	24	F	799341	N	N	N	N	N	N	N	N	-	-	9.3	92	4.9	9.3	18	0.8	21	28
CO	Mustafa	32	M	301358	N	N	N	N	N	N	N	N	-	-	9.4	96	4.5	9.4	22	0.8	21	32
CO	Munirathinam	35	M	876516	N	N	N	N	N	N	N	N	-	-	9.6	138	4.6	9.6	20	1	16	24
CO	Sathya	25	F	816527	N	N	N	N	N	N	N	N	-	-	9.5	108	4.4	9.5	19	0.5	26	38
CO	Uma	30	F	786924	N	N	N	N	N	N	N	N	-	-	9.2	96	4.8	9.2	26	0.9	16	34
CO	Arul	26	M	826595	N	N	N	N	N	N	N	N	-	-	8.9	56	4.7	8.9	24	0.9	24	30
CO	Sureshbabu	42	M	826597	N	N	N	N	N	N	N	N	-	-	8.5	62	4.8	8.5	22	0.7	14	26
CO	Balu	36	M	826609	N	N	N	N	N	N	N	N	-	-	9.3	72	4.7	9.3	16	0.6	16	32
CO	Chinnaponnu	36	F	826604	N	N	N	N	N	N	N	N	-	-	8.7	108	4.3	8.7	19	0.7	26	32

CO	Kuppan	45	M	526596	N	N	N	N	N	N	N	N	-	-	8.8	118	4.5	8.8	17	0.5	24	36
CO	Parrathi	44	F	15151	N	N	N	N	N	N	N	N	-	-	10.3	102	4.7	10.3	20	0.8	22	38
CO	Shanmugam	30	M	82587	N	N	N	N	N	N	N	N	-	-	9.6	97	4.7	9.6	21	0.8	29	34
CO	Jothi	28	M	826586	N	N	N	N	N	N	N	N	-	-	10.3	47	4.3	10.3	18	0.9	21	28
CO	Amsa	42	F	826580	N	N	N	N	N	N	N	N	-	-	9.5	89	4.7	9.5	18	0.9	16	23
CO	Sandhiya	20	F	862717	N	N	N	N	N	N	N	N	-	-	9.3	75	4.7	9.3	16	0.5	22	40
CO	Gajalakshmi	40	F	82659	N	N	N	N	N	N	N	N	-	-	8.9	128	4.3	8.9	20	0.8	18	26
CO	Rajathi	40	F	826395	N	N	N	N	N	N	N	N	-	-	9.5	92	4.3	9.5	17	0.9	18	26
CO	Rajgopal	20	M	826326	N	N	N	N	N	N	N	N	-	-	8.6	92	4.5	8.6	17	0.6	16	26
CO	Kumar	36	M	526882	N	N	N	N	N	N	N	N	-	-	8.8	56	4.4	8.8	24	0.8	22	28
CO	Rani	46	F	15298	N	N	N	N	N	N	N	N	-	-	9.2	64	4.7	9.2	20	0.8	16	32
CO	Lalli	40	F	321983	N	N	N	N	N	N	N	N	-	-	9.8	128	4.5	9.8	19	0.6	17	25
CO	Rajakumari	30	F	873261	N	N	N	N	N	N	N	N	-	-	10.5	112	4.7	10.5	17	0.9	14	26
CO	Nandhini	22	F	802806	N	N	N	N	N	N	N	N	-	-	9.8	96	4.6	9.8	17	0.8	18	26
CO	Kalai	38	F	799948	N	N	N	N	N	N	N	N	-	-	9.6	108	4.7	9.6	19	0.8	16	28
CO	Ushsrani	42	F	803314	N	N	N	N	N	N	N	N	-	-	9.6	62	4.4	9.6	13	0.6	14	28
CO	Rangaraj	46	M	45089	N	N	N	N	N	N	N	N	-	-	9.4	66	4.8	9.4	12	0.5	18	29
CO	Sekar	25	M	802990	N	N	N	N	N	N	N	N	-	-	9.6	107	4.7	9.6	19	0.8	18	32
CO	Deva	40	M	513276	N	N	N	N	N	N	N	N	-	-	9.8	96	4.6	9.8	19	0.5	16	25
CO	Venkatesan	33	M	808594	N	N	N	N	N	N	N	N	-	-	9.8	54	4.5	9.8	16	0.7	20	36

CO	Niranjani	28	F	811979	N	N	N	N	N	N	N	N	-	-	10.4	82	4.8	10.4	17	0.5	18	26
CO	Suriya	20	F	51691	N	N	N	N	N	N	N	N	-	-	9	48	4.7	9	24	0.8	17	26
CO	Dhanapal	45	M	51148	N	N	N	N	N	N	N	N	-	-	9.8	66	4.3	9.8	17	0.8	19	28
CO	Kothandam	40	M	818648	N	N	N	N	N	N	N	N	-	-	8.8	74	4.8	8.8	23	0.8	26	40
CO	Pandiyan	46	M	210593	N	N	N	N	N	N	N	N	-	-	9.5	126	4.3	9.5	19	0.5	17	28
CO	Naveendiran	19	M	827554	N	N	N	N	N	N	N	N	-	-	8.2	112	4.6	8.2	19	0.7	22	28
CO	Chinnathai	46	F	823548	N	N	N	N	N	N	N	N	-	-	7.6	120	4.8	7.6	20	0.5	22	28
CO	Nellammal	39	F	827619	N	N	N	N	N	N	N	N	-	-	8.1	124	4.9	8.1	22	0.9	22	29
CO	Magesh	36	M	825768	N	N	N	N	N	N	N	N	-	-	8.2	146	4.7	8.2	19	1	20	29
CO	Jothi	40	F	820171	N	N	N	N	N	N	N	N	-	-	7.8	106	4.4	7.8	28	0.7	22	29
CO	Jaya	25	F	82503	N	N	N	N	N	N	N	N	-	-	8.1	96	4.6	8.1	18	0.9	22	30
CO	Pomgavanam	26	F	326016	N	N	N	N	N	N	N	N	-	-	8.9	98	4.6	8.9	32	0.8	16	23
CO	Santhoskumar	40	M	826027	N	N	N	N	N	N	N	N	-	-	8.2	42	4.6	8.2	18	0.9	16	22
CO	Settu	33	M	55464	N	N	N	N	N	N	N	N	-	-	6.9	49	4.6	6.9	18	0.9	18	26
CO	Janaki	40	F	182767	N	N	N	N	N	N	N	N	-	-	8.2	147	4.1	8.2	28	1	25	28
CO	Peurumalsamy	43	M	827684	N	N	N	N	N	N	N	N	-	-	8.3	166	4.6	8.3	24	0.5	19	23
CO	Eswari	37	F	827685	N	N	N	N	N	N	N	N	-	-	8.3	182	4.7	8.3	20	0.8	22	19
CO	Isthiya	19	M	827689	N	N	N	N	N	N	N	N	-	-	8	114	4.3	8	23	0.9	29	22
CO	Radhabai	36	F	827609	N	N	N	N	N	N	N	N	-	-	8.1	58	4.7	8.1	19	0.8	33	29
CO	Venda	26	F	827700	N	N	N	N	N	N	N	N	-	-	8.4	78	4.6	8.4	14	0.5	16	20

CO	Amsa	35	F	827699	N	N	N	N	N	N	N	N	-	-	8.2	86	4.2	8.2	17	0.8	19	22
CO	Rajasekar	46	M	82772	N	N	N	N	N	N	N	N	-	-	8.1	92	4.8	8.1	20	1	22	28
CO	Karan	19	M	829715	N	N	N	N	N	N	N	N	-	-	8.4	106	4.5	8.4	24	0.7	26	21
CO	Vasanth	28	M	327673	N	N	N	N	N	N	N	N	-	-	8	153	4.3	8	16	0.7	16	22
CO	Karthiya	23	F	620816	N	N	N	N	N	N	N	N	-	-	9.2	148	4.6	9.2	18	0.5	23	27
CO	Raman	42	M	826060	N	N	N	N	N	N	N	N	-	-	8.1	105	4.9	8.1	17	0.9	26	21
CO	Sridhar	32	M	826068	N	N	N	N	N	N	N	N	-	-	8.3	92	4.3	8.3	20	1	18	23
CO	Kuppammal	40	F	826055	N	N	N	N	N	N	N	N	-	-	8.4	78	4.8	8.4	26	1	22	31
CO	Maniyan	45	M	828059	N	N	N	N	N	N	N	N	-	-	8.2	67	4.5	8.2	23	0.8	19	25
CO	Valli	32	F	826052	N	N	N	N	N	N	N	N	-	-	7.8	35	4	7.8	16	0.5	14	22
CO	Sankari	32	F	826058	N	N	N	N	N	N	N	N	-	-	10.5	186	4.9	10.5	20	0.4	29	17
CO	Rosy	35	F	826081	N	N	N	N	N	N	N	N	-	-	9.7	147	4.3	9.7	19	0.6	22	26
CO	Subramani	40	M	827524	N	N	N	N	N	N	N	N	-	-	8	96	4.6	8	28	0.7	20	26
CO	Kali	37	M	53205	N	N	N	N	N	N	N	N	-	-	9.1	56	4.6	9.1	19	0.8	18	36
CO	Raj	35	M	53995	N	N	N	N	N	N	N	N	-	-	8.6	193	4.6	8.6	19	0.5	22	46
CO	Pughazhendi	18	M	829824	N	N	N	N	N	N	N	N	-	-	8.6	199	4.2	8.6	32	0.9	36	15
CO	Devan	42	M	131672	N	N	N	N	N	N	N	N	-	-	10.1	149	4.8	10.1	23	0.8	25	33
CO	Damodaran	39	M	826066	N	N	N	N	N	N	N	N	-	-	8.7	163	4.3	8.7	20	0.4	19	23
CO	Soundar	32	M	861205	N	N	N	N	N	N	N	N	-	-	9.5	176	4.9	9.5	27	0.9	30	19
CO	Bhuvana	35	F	865321	N	N	N	N	N	N	N	N	-	-	8.8	143	4.5	8.8	30	0.6	18	27

CO	Manimagalai	42	F	826056	N	N	N	N	N	N	N	N	-	-	8.9	181	4.2	8.9	23	0.8	26	19
CO	Kanchana	38	F	617819	N	N	N	N	N	N	N	N	-	-	9.5	165	4.5	9.5	18	0.9	20	16
CO	Sukesh	19	M	602195	N	N	N	N	N	N	N	N	-	-	9.6	158	4.2	9.6	24	0.7	28	18
CO	Selvam	42	M	826015	N	N	N	N	N	N	N	N	-	-	10.2	147	4.8	10.2	20	1	29	21
CO	Gopal	42	M	610956	N	N	N	N	N	N	N	N	-	-	8.8	154	4.6	8.8	28	0.9	16	25
CO	Dharani	40	F	926814	N	N	N	N	N	N	N	N	-	-	8	175	4.7	8	19	0.8	18	25
CO	Suresh	38	M	926514	N	N	N	N	N	N	N	N	-	-	8.3	156	4.3	8.3	16	0.5	21	30
CO	Narayanasami	40	M	826051	N	N	N	N	N	N	N	N	-	-	7.9	46	4.3	7.9	18	0.5	17	21
CO	Vijayan	35	M	827716	N	N	N	N	N	N	N	N	-	-	8.3	53	4.8	8.3	22	0.6	27	21
CO	Mariya	19	F	827782	N	N	N	N	N	N	N	N	-	-	8	86	4.6	8	28	0.3	16	21
CO	Nivedha	20	F	826046	N	N	N	N	N	N	N	N	-	-	8.4	115	4.3	8.4	22	0.4	23	30
CO	Sajitha	21	F	826082	N	N	N	N	N	N	N	N	-	-	8	109	4	8	27	0.8	18	24
CO	Muneeswaran	44	M	826053	N	N	N	N	N	N	N	N	-	-	8.2	93	4.9	8.2	30	1	20	26
CO	Dharman	47	M	826058	N	N	N	N	N	N	N	N	-	-	8.3	75	4.6	8.3	21	0.6	24	18
CO	Venkateswaran	43	M	826052	N	N	N	N	N	N	N	N	-	-	8.1	62	4.7	8.1	23	.0.9	21	25

KEY TO MASTER CHART:

C	–	case
CO	–	control
Neck Sx	–	Neck Surgery
Pst Ac. Abd	–	Past Acute Abdomen
RAD	–	Radiation
HT	–	Hypertension
DM	–	Diabetes Mellitus
Alc	–	Alcohol
SD	–	Seizure Disorder
DUR	–	Duration
P	–	Phenytoin
PB	–	Phenobarbitone
CB	–	Carbamazepine
SV	–	Sodium Valproate
Ca	–	Calcium
ALP	–	Alkaline Phosphatase
Alb	–	Albumin
Co. Ca	–	Corrected Calcium
Cr	–	Creatinine
SGOT	–	Serum glutamic oxaloacetic transaminase
SGPT	–	Serum glutamic pyruvic transaminase
M	–	Male
F	–	Female
Y	–	Yes
N	–	NO

PATIENT CONSENT FORM

STUDY DETAIL: "A STUDY ON PREVALENCE OF MICROALBUMINURIA IN NON-DIABETIC PATIENTS WITH ACUTE MYOCARDIAL INFARCTION IN ICCU IN GOVERNMENT VELLORE MEDICAL COLLEGE HOSPITAL, VELLORE"

STUDY CENTRE:

PATIENT'S NAME:

PATIENT'S AGE:

IDENTIFICATION NUMBER:

I confirm that I have understood the purpose and procedure of the above study. I have the opportunity to ask questions and all my questions and doubts have been answered to my complete satisfaction.

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected.

I understand that the sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However I understand that my identity would not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study.

I hereby consent to participate in this study.

I hereby give permission to undergo complete clinical examination and diagnostic tests including haematological, biochemical, radiological tests.

Signature/thumb impression:

Patient's name and address: Place: Date:

Signature of the investigator:

Name of the investigator: Place: Date

மாதிரிப்படிவம்

ஆராய்ச்சித்திட்டத்தலைப்பு :

முழுப்பெயர் :

தற்போதை / தொடர்புமுகவரி :

பாராளுமன்றத் / வலை :

I. நான் மேலே குறிப்பிட்டுள்ள ஆராய்ச்சி குறித்த விளக்கம் உள்ளடங்க படித்துபுரிந்து கொள்ளப்பட்டது நான், எனக்கு மகளிர்மருத்துவ விளைவு அளிக்கப்பட்டது நானாக முன்வந்து சம்மதிக்கிறேன்.

II. நான் இந்த ஆராய்ச்சியில் பங்குகொள்வது தன்னிச்சையானது நான் நானாக, நான் எப்போதுவேண்டுமானாலும், காரணம் மற்றும் எதிர்விளைவுகளின்றி இந்த ஆராய்ச்சியிலிருந்து விலக முடிவு எடுக்கும் உரிமை நானாக, அப்படி விலகுவதனால் நான் சட்ட ரீதியான மற்றும் சமூகரீதியான பாதிக்கப்படமாட்டேன் நானாக நான் அறிகிறேன்.

III. இந்த ஆராய்ச்சியில் புரவலர் மற்றும் அவரது சார்பான பணிபுரிபவர்கள் விற்றுமுதல்களின் குழு மற்றும் கூடுபாடு குழுவினர் ஆகியோர், இந்த ஆராய்ச்சியில் எனது, பணியை இதனுடன் தொடர்புடைய ஆராய்ச்சி விசயங்களை எனது அனுமதி இல்லாமல் காண அனுமதி அளிக்கிறேன். முன்னாள் நபர்களுக்கு இந்த ஆராய சிசியை பார்க்க விளக்கம் எனது, இந்த ஆராய்ச்சியில் முடிவுகளை பார்க்கவும் எனது அனுமதி அவசியமில்லை விளக்கப்பட்டது நானாக நான் அறிகிறேன்.

IV. இந்த ஆராய்ச்சியில் முலம் அறியப்படும் விஷயங்கள் மற்றும் முடிவுகள் அறிவதால் சார்ந்த காரணங்களுக்காக விளக்கப்பட்ட படுவதை நான் எப்போதும் தடுக்கலாம்மென் நானாக உரிமை அளிக்கிறேன்.

V. நான் இந்த ஆராய்ச்சியில் பங்கு பெறுகிறேன் எதிர்பார்க்கிறேன்.

1) ஆராய்ச்சியில் பங்கு கொள்பவர் / சட்டப்பூர்வ பிரதிநிதியின் கையெழுத்து / ஆள்காட்டி விரல் பதிப்பு

பெயர் / உறவுமுறை

2) ஆராய்ச்சியாளரின் சாட்சி கையெழுத்து, தேதி